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TWO CASES OF CONGENITAL ANOMALIES OF THE BRAIN

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Some years ago this journal published a report of my observations on three children presenting congenital hypertrophy of the muscles, extrapyramidal motor disturbances and mental deficiency.[1] The report also cited a fourth case, found in the literature. After the death of the first child examination of the brain was possible. Underdevelopment or inhibition of the striatum, especially the neostriatum, was observed. Moreover, there was a widespread porencephalic process, regarded as secondary. In my opinion the four children presented in their symptoms a clinical entity, though it is not yet possible to explain the relationship between the malformation of the striate body and the muscular hypertrophy.

Since publication of the article, there have been sent to the Children's Clinic of the University of Amsterdam two infants considered by the attending physicians as having the same triad of symptoms. Though the diagnoses are not accepted as entirely correct, the two cases somewhat resemble those reported earlier. Autopsy of one of the recent patients, together with microscopic examination of the brain, was permitted. The histories and the laboratory findings for the two children recently seen will be given here.

The children described by Debré and Sémelaigne [2] were of a distinctly different type. Those children suffered from congenital myxedema or sporadic cretinism with hypertrophic, or rather pseudohypertrophic, muscles. In the clinic I saw several such patients, and reports of cases similar to theirs have been made by Langhans (who also reported

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1. de Lange, C.: Congenital Hypertrophy of the Muscles, Extrapyramidal Motor Disturbances and Mental Deficiency: A Clinical Entity, Am. J. Dis. Child. **48**:243 (Aug.) 1934.

2. Debré, R., and Sémelaigne, G.: Arch. de méd. d. enf. **38**:516, 1935; Syndrome of Diffuse Muscular Hypertrophy in Infants Causing Athletic Appearance: Its Connection with Congenital Myxedema, Am. J. Dis. Child. **50**:1351 (Dec.) 1935.

on microscopic examinations), Dieterle and Wieland.[3] Extrapyramidal motor disturbances are lacking here, and the administration of thyroid proves a great success. So it is surprising that Debré has persisted in his opinion that the triad of symptoms presented in my earlier article represented an unrecognized myxedema, the extrapyramidal motor disturbances seeming to him to be of little or no interest, whereas they are in reality one of the three symptoms *sine qua non* and are therefore of fundamental importance.

Contrary to Debré's belief, it is easy to recognize the differences between the pictures he gave of his patients and those given of mine, the former having typical congenital myxedema.

REPORT OF CASES

CASE 1.—A., a girl, was born prematurely, at seven months, on Jan. 25, 1933. Her weight at birth was 1,600 Gm. The mother also had been a premature infant. She was mentally backward but had seemed only slightly so until the time of her marriage. Since then she had become much worse. Her husband was a drunkard. Before the birth of the child under consideration here, another premature infant weighing 1,500 Gm. was born, and developed normally. The first three children of the marriage were born at full term and were normal.

When infant A. was 2½ months of age a gradually increasing rigidity of the body was noted. At the age of 5½ months the child was sent to the outpatient department of the clinic, and the following observations were made.

The child was small and of dystrophic appearance with a low forehead and a slightly protruding occiput. The head was bent far backward. It was possible to bring the child's chin down to touch the chest, but the head resumed its former position as soon as the hand of the examiner was withdrawn. The muscles were hypertonic; now and then the tonus lessened somewhat. On both sides of the body the deltoid, the biceps brachii, the triceps brachii, the pectoralis major and the triceps surae muscle were clearly visible. The tonus of the muscles of the buttocks was less marked. There were no symptoms of involvement of the pyramidal tracts. The thick, short neck and the hypertrophic tongue, which are characteristic of children with the triad of symptoms previously mentioned, were lacking, and the muscles were thought to be in a state of hypertonus and not of hypertrophy. There was no malformation of the ears. Examination of the chest and the abdomen revealed no abnormalities. No nevi or angiomas were present.

A tentative diagnosis of a cerebral disorder, probably involving the striate body, was made.

The child was returned to her native village, and no additional symptoms were noted except that she was observed to be mentally backward. On Oct. 14, 1933, at the age of 8½ months, the patient died of erysipelas. Postmortem examination of the cranium only was possible and was made by Dr. D. E. Schouten. The falx cerebri proved to be absent in the forepart of the brain. A mass of blood vessels was situated on the spot where the olfactory nerves left the brain. By courtesy of the attending physician (Dr. C. H. J. van Lohuizen) I was permitted to examine the brain in Professor Brouwer's neurologic lab-

3. Langhans, T.: Virchows Arch. f. path. Anat. **149**:155, 1897. Dieterle, T.: Jahrb. f. Kinderh. **64**:465, 1906. Wieland, in von Pfaundler, M., and Schlossmann, A.: Handbuch der Kinderheilkunde, ed. 4, Leipzig, F. C. W. Vogel, 1931, vol. 1, p. 1002.

oratory. The weight of the cerebrum was 460 Gm. after it had been hardened in a 10 per cent dilution of the standard solution of formaldehyde (40 per cent).

Macroscopic Appearance.—There was an extensive conglomeration of blood vessels at the base of the frontal lobes and passing onto the dorsal side. This conglomeration was situated in the pia-arachnoid but did not reach the brain itself (fig. 1).

In the frontal part of the dorsal side the hemispheres were grown together. This could not have been the effect of secondary meningeal involvement, for a caudal part of the first frontal gyrus stretched across to the other side (fig. 2). There was polygyria of the frontal lobes. On the left the sulcus centralis Rolandi did not cut into the mesial side. The sylvian fossa could be traced. The insula was not lying free. On the right neither the sylvian fossa nor the sulcus centralis could be identified with certainty. The temporal lobes were well developed. The first temporal gyrus reached to both sides of the occipital lobe.

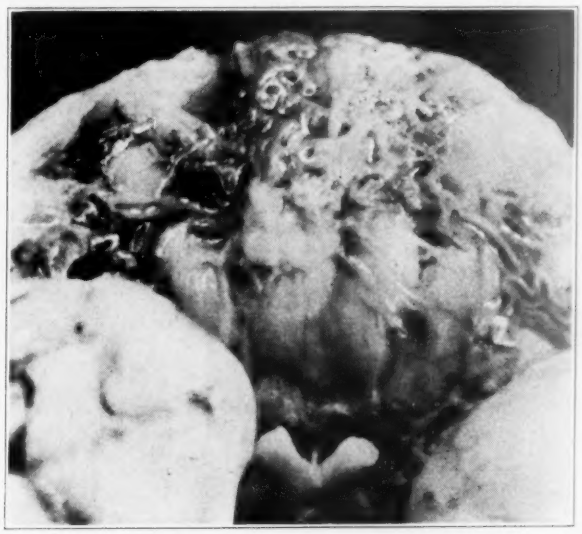

Fig. 1 (case 1).—Conglomeration of blood vessels at the base of the frontal lobe.

The optic nerves and the optic chiasm appeared normal, and the infundibulum did not protrude. The region of the cisterna magna was enlarged. The pons was well developed, as were the pyramids, the inferior olives and the cerebellum.

The brain stem was cut off through the pedes pedunculi and through the caudal part of the anterior corpora quadrigemina. The aquaeductus Sylvii was open.

The cerebrum was cut into frontal sections. The first frontal section extended through the anterior part of the uncus. The corpus callosum, the septum pellucidum and the anterior portion of the fornix seemed to be lacking. The lateral ventricles were relatively small. The capsula interna ran in a horizontal direction. The centrum semiovale was small. In the mass lying underneath the capsula interna it was not possible to distinguish clearly between the putamen and the globus pallidus.

The second frontal section passed through the middle of the optic chiasm, through the optic thalamus where it is largest, through the tractus opticus and through the infundibulum. There was only one anterior ventricle; the septum pellucidum and the corpus callosum both were lacking. It was clear that the deep mesial dorsal fissure was absent. A large gyrus lay dorsal to the ventricle.

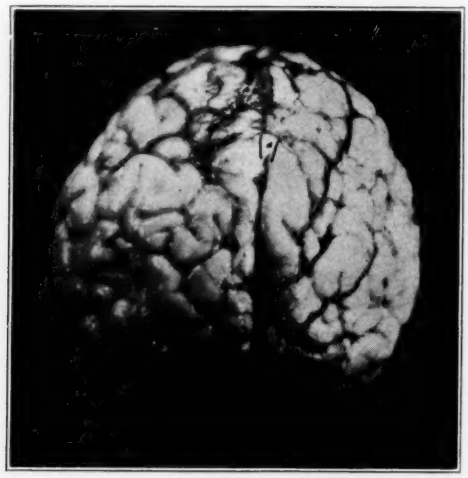

Fig. 2 (case 1).—Crossing gyrus. It is marked with a dot between two vertical lines.

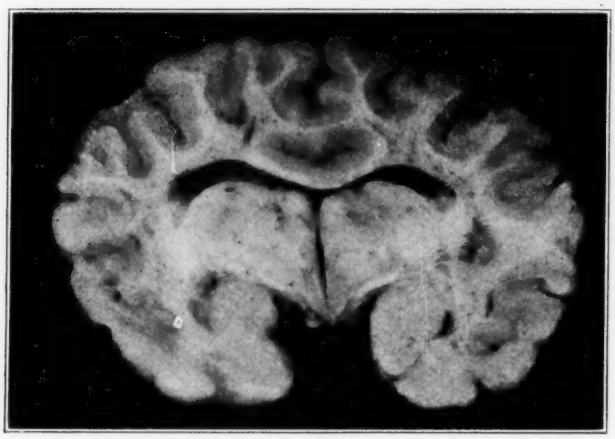

Fig. 3 (case 1).—Second frontal section.

In comparison with the thalamus the pallidum seemed small. The third ventricle had a normal aspect, as did the pars retrolenticularis of the capsula interna and the nucleus lentiformis. On both sides the centrum semiovale was small. Figure 3 presents this section.

The third frontal section extended through the part in which in the normal brain the splenium corporis callosi is situated. The splenium seemed not to be totally absent; on both sides the calcarine fissure seemed to be present.

Microscopic Technic.—Sections from several parts of the cortex of the cerebrum and the cerebellum were embedded in paraffin and stained by various methods. Sections of the conglomeration of blood vessels and of the striate body also were so treated, and frozen sections of the latter were prepared by Bielschowsky's method.

Finally the frontal poles were cut off and the different parts into which the brain had been divided by the frontal sections were put into Müller's solution, embedded in pyroxylin and cut into serial sections measuring from 30 to 35 microns. Some sections were stained by the Weigert-Pal method, and others by the Van Gieson method.

Fig. 4 (case 1).—Large sized capillaries in the inflamed pia-arachnoid.

Microscopic Examination.—Meningitis, probably a part of the erysipelas to which the child had succumbed, had spread over the whole brain, though its manifestations differed somewhat in various parts.

There was a conglomeration of blood vessels in the pia-arachnoid lying on the first frontal gyrus. The vessels had thin walls, like those of capillaries, but the lumens were much larger (*Reisenkapillaren Aschoff*). They were surrounded by cuffs of inflamed cells and lay in the inflamed pia-arachnoid (fig. 4). Streptococci were seen. The superior layers of the gyrus showed vessels surrounded by leukocytes.

The second frontal gyrus showed a broad lamina zonalis and two granular layers.

In the crossing frontal gyrus there were an external and an internal granular layer. The third layer was thick but contained only a small number of ganglion cells, which were shrunken or poorly developed.

In the right temporal lobe there was a broad lamina zonalis, and in the third and the fifth layer were well developed ganglion cells in undiminished quantity.

The right motor region showed an internal granular layer. The Betz ganglion cells were present only in small numbers.

In the right occipital lobe was a broad lamina zonalis. There was separation of the third layer into one lamina with small cells and another with larger cells.

In different parts of the vermis cerebelli the external granular layer was still present. The Purkinje cells looked normal. In the medulla some ganglion cells were visible.

The right and the left hemisphere of the cerebellum appeared normal, and the external granular layer was for the most part present.

In idiotic children an internal granular layer is often found in the motor region; such a layer is lacking in the normal brain. Also the brain of a young

Fig. 5 (case 1).—Coherent medullar mass.

child, up to several months of age, may show an internal granular layer. The presence of such a layer in the motor region may be regarded as a sign of retardation, and the same holds true of the internal granular layer in the second frontal gyrus.

The cerebellar cortex was normal for a child 8½ months of age.

The ganglion cells in the striate body were well shaped, and their number did not appear smaller than in control preparations.

In the serial sections it was clear that there was present not only meningitis but encephalitis, which spread deeper into the brain than is the case with the ordinary border encephalitis accompanying meningitis.

The frontal poles were not separated, and they were surrounded by a conglomeration of blood vessels. There was polygyria of the frontal portion of the brain. The dorsal part of the medulla cerebri covered only a small area, but ventrally there was a coherent medullar mass stretching in a horizontal direction (fig. 5). On serial examination of the sections, in a frontal-caudal direction, the medulla appeared to thicken gradually to form the centrum semiovale. There was only one such center, the right and the left being united. Also it was noted that the small united mass in the middle gradually broadened.

The corpus callosum, the radiation corporis callosi, the fornices and the septum pellucidum were absent. The myelinated fibers lying in the middle faintly resembled the radiation corporis callosi, but were in reality an undifferentiated mass (fig. 6).

No gyrus callosomarginalis could be identified; the cingula and the strata were lacking. There was no longitudinal callosal bundle such as is usually seen in a brain which lacks the corpus callosum and is to be considered a collection of noncrossing callosal fibers.[4]

There was displacement of several parts of the brain stem and the pallium in relation to one another. For instance, on serial examination of the sections from front to back, the putamen appeared on both sides before the nucleus caudatus was seen and long before the horn of the lateral ventricle showed. Contrary to the normal aspect, the beginning of the ventricle was visible in sections in which the temporal lobe was not yet seen. As figure 7 shows, there was only one lateral ventricle, and there seemed to be a coalescence of the nuclei caudati. This, however, was not the case, for on microscopic examination there was seen a fissure between them which ran in a basal direction to the point at

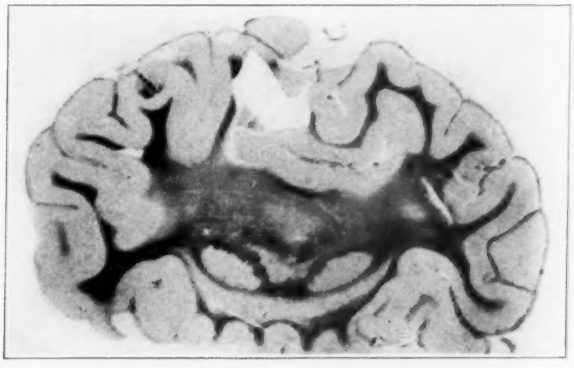

Fig. 6 (case 1).—Undifferentiated mass of myelinated fibers in the center.

which in the normal brain the connection between the two is found. Dorsally the fissure was wholly filled with connective tissue and small round cells, and there were also small holes lined with ependymal cells and nests of the same cells, which were remnants of ependymitis of long standing. Such holes were present also along the border of the anterior horn of the one lateral ventricle. There the blood vessels showed no cuffs, and there were no agglomerations of small round cells, which facts are in accordance with the hypothesis that the inflammatory process was an old one. However, when in the course of examining the sections the third ventricle was reached, the fissure was observed to be partly open, though for not more than a hair's breadth, and in this basal part there was an acute inflammatory process—recent encephalitis. The ependyma of the third ventricle showed a new inflammation. These processes of recent origin were part of the meningitis to which the child had succumbed. There was no ependymitis of the middle and the posterior horn.

The claustra were united in the middle by fairly vigorous fibers which belonged to the external capsule and which at this point formed the most basal

4. de Lange, C.: J. Nerv. & Ment. Dis. **62**:449, 1925.

part of the brain. This gave a peculiar appearance, the more so as only a small beginning of the temporal lobes was seen in the same sections of the brain. It looked as if the base of the cerebrum was much more deeply excavated than it is in normal circumstances. This is explained by the fact that the rhinencephalon was displaced in a caudal direction. The rhinencephalon was only moderately well developed. The myelin sheaths of the fibers of the centrum semiovale were sparse or altogether lacking, but there were no symptoms of degeneration of the sheaths; so it must be concluded that they were lacking originally or that their development had been interrupted.

On comparing a section of a normal brain embracing the beginning of the corpora mamillaria with a section from the same region in the brain under examination the displacement already mentioned was clearly seen. In the normal brain were seen the beginning of the thalamus opticus and Vicq d'Azyr's bundle, the nucleus amygdalae, large parts of the nucleus caudatus, the globus pallidus with two lamellae and the beginning of the middle horn. In the section taken

Fig. 7 (case 1).—The one lateral ventricle.

from the brain of the patient were embraced the red nuclei, the pulvinar, the pedes pedunculi and a wide lumen of the middle horn. The fissure which between the nuclei caudati was filled with products of the inflammatory process deepened and broadened as the third ventricle appeared in succeeding sections and gradually came to appear empty. Above the anterior horn of the lateral ventricle a bundle of myelinated fibers was seen which had a faint resemblance to a callosal formation. Microscopic examination, however, showed that the fibers did not run transversely. The cingula were lacking. The well shaped capsula interna ran in a horizontal direction throughout its course.

The third ventricle had a deep, narrow infundibulum. The anterior commissure was wholly lacking, but the other commissures were well developed, as were the bundles of Vicq d'Azyr and Meynert. The thalami nervi optici, with the taenia thalami, were well formed. The various nuclei appeared normal, as did the *Gitterschicht* (fig. 8). The position of the thalami nervi optici were almost horizontal.

In sections showing the caudal part of the pulvinar the fimbria on both sides could be traced; however, since the fornices were lacking conjunction had not taken place. The fascia dentata, the nucleus ruber, the nucleus amygdalae, the gyrus hippocampi, the cornu ammonis, the corpus mamillare and the geniculum on both sides were well developed.

The frontal parts of the pyramidal tracts and the substantia nigra also had a normal appearance.

In examining sections of that part of the brain where normally the splenium corporis callosi is situated, fibers running tranversely were seen. These probably represented a kind of splenium. No forceps major could be made out with certainty, but the forceps minor was traceable. The strata of the posterior horn were

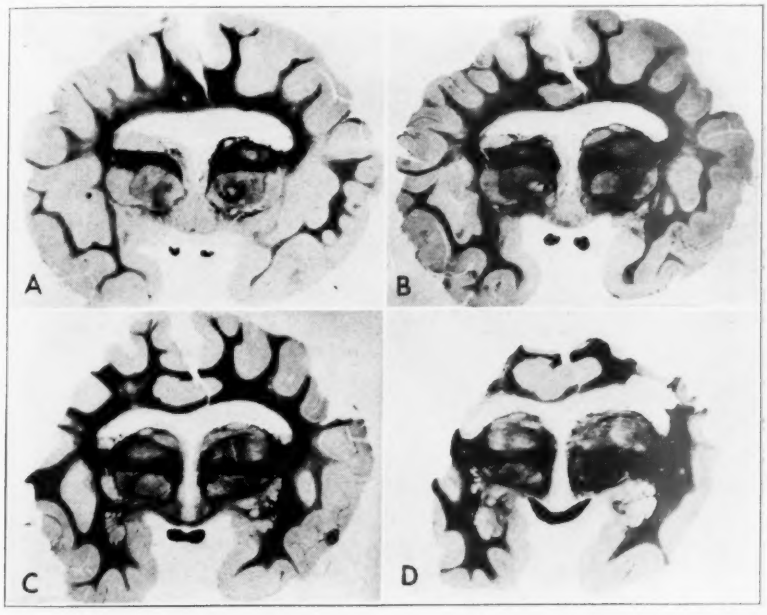

Fig. 8 (case 1).—Cross-sections showing bundles of the globus pallidus at their point of origin.

visible. A bundle of fibers showed there on each side and perhaps may be interpreted as the cingulum. The calcarine fissure looked normal. The parieto-occipital fissure was shallow. Otherwise the occipital lobes looked normal.

As for the striate body, it already has been stated that in reviewing sections in a frontal-caudal direction the putamen was reached long before the ventricle, which is contrary to normal. The striate body was, however, of hypoplastic build and appeared pale in sections stained by the Weigert-Pal method. On comparing these sections with others stained by Van Gieson's or Apathy's method it was seen that the number of fibers was not particularly small but that the myelinization was defective or lacking. This held true for the finer as well as for the coarser fibers. The ganglion cells were rather sparse, but their aspect was normal. The nucleus caudatus was of ordinary size, but its myelinization was defective. The small ganglion cells were fairly numerous; the larger forms were somewhat diminished in number.

The globus pallidus was really hyperplastic, rather than merely appearing so in comparison with the reduced putamen, and its fiber reticulum was dense. In some places the fibers were in nestlike arrangement. The lamina externa was well developed and of normal aspect. The lamina interna in the more caudal parts of the globus had more or less the form of a ring. The bundles passing into the globus pallidus from the putamen and the nucleus caudatus showed pale in the sections stained by the Weigert-Pal method. This fact was in accord with the aspect of the bundles at their points of origin (fig. 8). The ansa lenticularis was well developed. The ganglion cells in the globus pallidus appeared normal.

Examination of the brain stem proved the anterior and the posterior corpora quadrigemina, the posterior longitudinal fasciculus and the aquaeductus Sylvii to be of normal aspect.

The nuclei pontis were displaced, and they appeared in the same sections as the pyramid and the nucleus arcuatus (fig. 9).

The meningitis had spread over the cerebellum, which otherwise showed nothing abnormal.

It seemed possible that the angioma had influenced the formation of the frontal poles of the brain and that the coalescence of those parts had in turn influenced the development of other parts and caused their displacement. However, in view of the hypertrophy of the paleostriatum and the normal state of the nucleus amygdalae, the underdevelopment of the neostriatum cannot be explained in this way.

It is not surprising that, together with the symptoms of recent meningitis and encephalitis, the brain presented the vestiges of an inflammatory process of longer standing. It is well known that a malformed brain is particularly likely to become inflamed, the process sometimes beginning in fetal life. Neither is it astonishing that, notwithstanding the malformation of the centrum semiovale, the capsula interna and the pyramidal tracts were fairly well developed.

In children or in experimental animals it has been observed that if certain parts of the brain degenerate or are destroyed, those parts closely related to them degenerate also. On the other hand, in the malformed brain it is often noted that processes of retardation in certain regions are not associated with underdevelopment of those parts which after the occurrence of an extra-uterine pathologic process are dependent on them. In the fetal brain the different regions have a large measure of independence in their development.

The question arises whether the anatomicopathologic findings in this case fully explain the clinical picture. It is well known that degeneration of the globus pallidus produces a severe degree of rigidity. One is entitled to regard the hypertrophy of the globus pallidus, with its nestlike arrangement of fibers, as a malformation which must have inhibited the normal function of the organ.

CASE 2.—B., a boy, was born at full term on Jan. 31, 1935, with incomplete breech presentation. His weight was 2,870 Gm., and his length, 51 cm. He was born in the Maternity Hospital and, being not quite normal, was transferred

to the ward of Dr. N. I. Heybroek, consulting pediatrist for the hospital, to whom I am indebted for the following details. The child was extremely active. The head was bent backward, and the back was in opisthotonos. The legs were

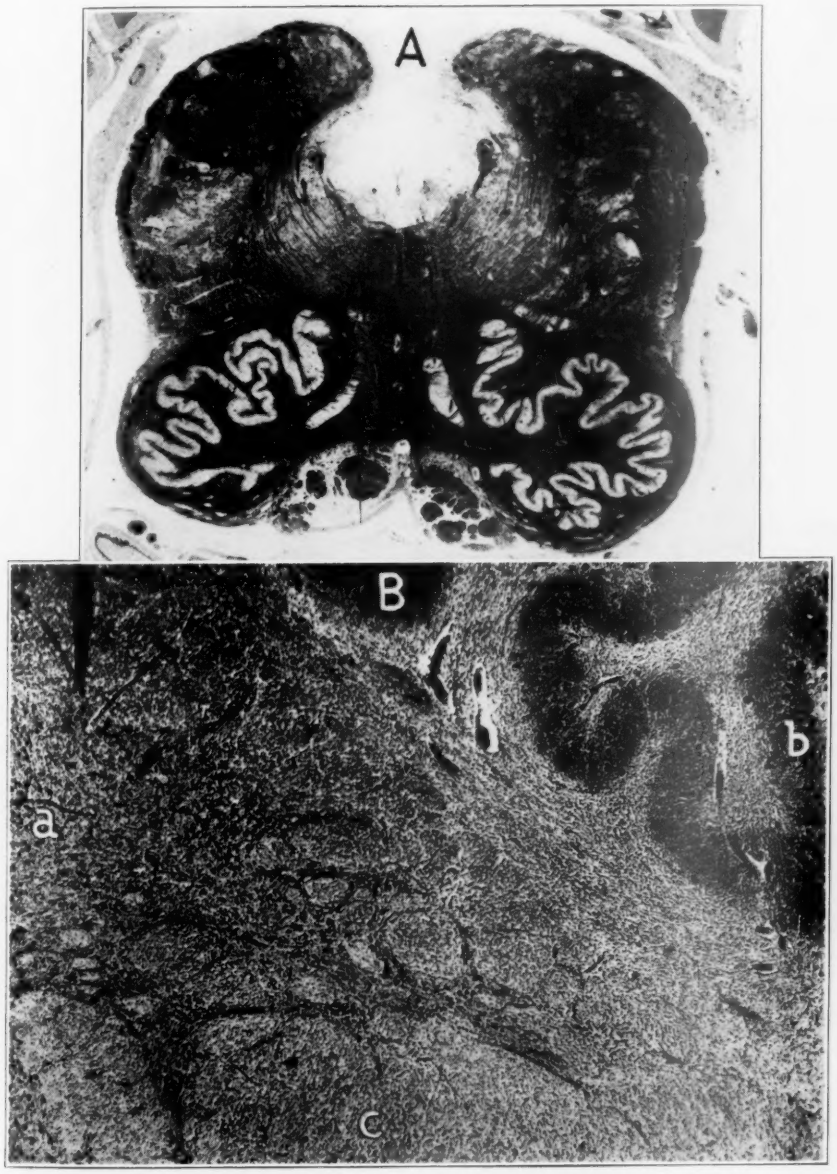

Fig. 9 (case 1).—*A* shows the nucleus pontis, the pyramid and the nucleus arcuatus. *B* shows part of the same section on a larger scale: *a*, the nucleus pontis; *b*, the inferior olive, and *c*, the pyramid.

rigidly extended. The anterior fontanel did not bulge, and there were no convulsions. Examination of the heart, the lungs and the abdomen proved them to be normal. Lumbar puncture was made on February 9, but there was no fluid. A Wassermann test of the blood gave negative results. During the next several weeks the rigidity and the opisthotonos increased. The child lay in a bridgelike attitude, with his heels and the back of his head for pillars. Several muscles which at birth had not shown stood out and became hypertrophic. The child lost weight, and on April 1, 1935, he was sent to the pediatric department, with the diagnosis of congenital hypertrophy of the muscles, extrapyramidal motor disturbances and mental deficiency ("athlete's or wrestler's triad").

The child's face, however, did not resemble the faces of children with those symptoms. It was the face of a normal infant, without the look of idiocy or the hypertrophic tongue. The ears were large but presented no malformation. The child showed great activity. His cries did not at all resemble the wail, like a swelling and dying siren, which is peculiar to infants with malformation or developmental retardation of the striate body. The head was bent far backward. The chin could easily be brought into contact with the chest, but as soon as the pressure was removed the head resumed its former position. The neck was thick but not short. The child's appearance was decidedly dystrophic, and his face had a grayish hue. During the examination the patient was mobile and restless, and his face wore an expression of displeasure. His voice was clear and his crying vigorous. In crying the expirium was quickly cut off, and the inspirium was slightly stridulous. The pupils of the eyes reacted to light. The eyeballs were generally turned up, showing the white of the eye below the cornea but not above it.

The skin was loose, almost all the subcutaneous fat having disappeared. The hypertonic musces showed clearly beneath the thin skin. One received the impression that some groups of muscles (the deltoid, the brachioradialis, the triceps surae and the quadriceps femoris) might be slightly hypertrophic. They stood out and felt hard. The same did not hold true for the glutei or the muscles of the abdominal wall. When the child was quiet the legs were generally stretched out, the arms were crossed over the upper part of the abdomen and the hands were clenched. When he grew restless the opisthotonos increased to such an extent that he lay in an *arc de cercle*. The legs were stretched rigidly backward; the arms executed slow thrusting and waving movements, and the hands made clutching gestures. While making these motions the child cried, and soft swellings appeared before and behind the sternocleidomastoid muscles and in a lesser degree also in the neck. They bore a faint resemblance to an enlarged thyroid gland but probably represented a mass of engorged blood vessels and muscular and fatty tissue. This is a phenomenon which now and then can be observed in healthy young infants also. When the child became quiet the swellings disappeared. The maximum hyperextension came in fits of a convulsive character, accompanied with clonic extension of the arms and the legs. At such times there was hypertonia of the whole body. All the child's reflexes were lively, but there were moments when they could not be elicited, because the hypertonia was too strong. Sometimes clonus of the knee and of the Achilles tendon were present. Neither clasp-knife rigidity nor the cogwheel phenomenon was clearly shown. Figure 10 shows the appearance of the child when he was admitted to the clinic.

As to sensibility, it always is difficult to make accurate observations on young children, but it was clear that wherever it was tried a pinprick gave the patient a disagreeable sensation.

Fovea coccygea and slight hypertrichosis of the sacral region were noted. The lines in the palms of the hands were normal, except that the grooves were unusually deep. The lines in the soles of the feet were especially deep. An abnormal groove ran from the base of the third toe in the direction of the heel, and there were many extra, small lines (fig. 11).[5] Roentgenograms of the skull, of the cervical part of the spine and of the thorax showed no unusual features. The fundus oculi was normal.

Lumbar puncture yielded a normal fluid, except that the sugar content was somewhat high. The pressure was normal. Examination of the muscles by application of a galvanic current revealed no anomalies, and examination of the blood and the urine proved them to be normal.

Soon after the child's admission to the clinic a large prolapsus ani developed.

Fig. 10 (case 2).—Child as he appeared when admitted to the clinic.

Only the salient points of the history of the case will be mentioned here.

On May 5, 1935, the child's weight had increased and his general condition had improved. The reflexes were lively if hypertonia did not prevent their being elicited. There was spasm of the adductor muscles, and the child crossed his legs when he was grasped at the armpits and held upright. The cogwheel and the clasp-knife phenomena were not noted, but after the examiner made passive flexing movements with the child's limbs, the child himself was able to flex his arms and legs much more smoothly.

On the night of May 19 the child had a convulsion.

5. In mentally backward children often there are anomalies of the lines of the hand and the foot. De Lange, C.: Maandschr. v. Kindergeneesk. **4**:9, 1935.

On June 14 it was recorded that the feeding of the patient presented a difficult problem. The child would lie on his abodmen, in the nurse's lap, his back hollow and his head bent far backward. Small quantities of food could be dropped cautiously into his mouth from a spoon.

On July 1, the child's weight was 3,490 Gm. It appeared that several muscles which were in almost constant use had become slightly hypertrophic. This also held true for the muscles of the abdominal wall, which at first had not stood out. However, it is difficult to distinguish in a thin child between hypertonia and a slight degree of hypertrophy. The arms were generally bent at the elbows but could be passively stretched out without the exertion of much force. The triceps reflex was lively, as were the knee jerk and the Achilles tendon reflexes. In both feet the sole reflex was lacking, or the Strümpell reflex was elicited. On percussion above the tibia, however, dorsal flexion of the foot resulted, with extension of the great toe and sometimes with spreading of the other toes.[6]

Fig. 11 (case 2).—Abnormal lines in the soles of the feet

On August 1 it was noted that now and then the child lay in a more normal attitude than formerly. Though his facial expression did not give at all the impression of idiocy, he was decidedly backward. His general somatic condition was much improved.

On October 10, at the age of 8 months, the child had a healthy color and had become noticeably quiet. His weight was then 5,530 Gm. (fig. 12). A diagnosis of true hypertrophy of the muscles could not be made, though most of the muscles felt hard. In general the patient's accustomed position had improved; now and then he was found lying in his crib as does a normal child, but there still were moments when he held the *arc de cercle* position. If he was held by the occiput he could be brought into a sitting position. It was not possible, however, for him to stand upright, supported in that way, for when it was attempted he sagged at the knees.

6. I have observed the latter reflex also in two infants suffering from hydrocephalus.

The pupils of the eyes were somewhat narrow, but they reacted to light. The eyes appeared not to follow a moving object, at least not in an upward or downward direction, though now and then it seemed as if the eyes followed the object when it was moved to the right or the left. The menacing reflex was lacking, which perhaps was still normal for the child at that age. The expression of his face was one of apparent contentment, but he had never once laughed. It was no longer necessary that he lie on his abdomen while being fed; the nurse could hold the child in her arm and feed him in the ordinary way.

The anterior fontanel measured 6.5 by 6.5 cm. and was somewhat bulging. The posterior and the lateral fontanel were still open. The coronal suture was not yet wholly closed. Yet there was practically no rickets. The greatest circumference of the head was 41.5 cm. With the child in a better condition somatically, his throat looked much more nearly normal. The swellings were no longer seen.

Fig. 12 (case 2).—Child at the age of 8 months

The child's arms were usually bent at the elbows, and it was more difficult to stretch them out than it had been some weeks earlier. The fingers also were bent, but it was easy to bring them into a different position. All the reflexes were still lively. There was no longer a spasm of the adductor muscles or a crossing of the legs when he was grasped at the armpits and held upright. There was no clonus of the Achilles tendon or of the knee and no great toe reflex. A previously mentioned reflex—dorsal flexion of the foot when the leg was struck above the tibia—was still present. There was no contralateral reflex of the adductor muscles. There were no Magnus de Klejn reflexes.

Later the prolapsus ani, which had become less serious, again gave much trouble. The child had slight convulsive movements and fever for a few days.

On October 23 lumbar puncture was made. The pressure had not increased, and the reactions were negative, save for a feeble positive reaction to the Nonne test. The number of cells was not increased. The reactions of the spinal

fluid to the Wassermann and Sachs-Georgi tests were negative. Even before the lumbar puncture was made the anterior fontanel bulged less than it had earlier. After the puncture it became flat, but it soon bulged again.

On November 2 it was recorded that the fever persisted. The child was restless and cried loudly. This was followed by profuse sweating and convulsions.

On November 3 there was hyperthermia.

On Novmeber 4 death occurred. There was no evidence of a pathologic condition in the internal organs. Postmortem examination was not permitted. During the whole of the patient's stay in the hospital he now and then had a temperature above normal, which was probably due to the cerebral condition.

This child either had a congenital cerebral anomaly or suffered from an injury which occurred at birth, the lesion in either instance involving the pyramidal tracts. In favor of the theory of a congenital anomaly were the concomitant fovea coccygea, the hypertrichosis in the sacral region and the abnormal lines in the soles of the feet, since it is well known that often several anomalies occur in the same person. Hypertonia was pronounced and there was possible slight hypertrophy of the muscles due to overuse (i. e., the constant and exaggerated contractions). The symptoms make it probable that there was also meningo-encephalitis or ependymo-encephalitis of extra-uterine origin, causing a mild degree of hydrocephalus.

Symptoms of extrapyramidal involvement could not be recognized with certainty. As for the opisthotonos and for the facts that there was a striking variability in its degree and that it became positively less in the later months, a valid explanation is lacking.

Although the symptoms showed some resemblance to the triad previously mentioned, they were not identical with them.

In spite of the fact that anatomicopathologic examination of the brain was not possible, the history of the case is given here, since it may furnish comparative notes for future clinical observations in cases in which permission for postmortem examination is granted.

Attention is drawn to the peculiar reflex of the lower part of the leg.

SUMMARY

Any relation between the triad of symptoms—congenital hypertrophy of the muscles, extrapyramidal motor disturbances and mental deficiency—and congenital myxedema is strongly denied.

Two cases are analyzed in which the patient was sent to the clinic after diagnosis of the group of three symptoms mentioned. The reasons that the diagnoses could not be accepted as correct are given.

THE LIPIDS OF THE BLOOD PLASMA IN THE NEONATAL PERIOD

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A review of the literature reveals no complete study of the blood lipids of new-born babies. Isolated analyses for individual lipids, usually cholesterol or lipid phosphorus or occasionally both, during the neonatal period have been reported frequently and the results compared with values for older children, normal adults and pregnant women. The methods employed in these isolated measurements have been criticized by several authors, most recently by Boyd,[1] Kirk, Page and Van Slyke[2] and Sperry.[3] This study was undertaken to establish a range of values for the total lipids and for each of the lipid components of the blood plasma of normal infants during the neonatal period, using methods which obviated most of the criticisms of the older procedures.

SUBJECTS

The twenty-five normal full term infants used in this study were born in the lying-in pavilion of the New York Hospital of mothers who had had uncomplicated pregnancies and uneventful deliveries, with nitrous oxide as the anesthetic, supplemented in fourteen cases with a small amount of ether. Two or more determinations of the lipids were made on each infant during the first two weeks of life. The first analysis was made on the day of birth, from one to twelve and three-fourths hours after delivery and before the ingestion of food; the second, from six to ten days later, at a time when the birth weight was being regained and in the absence of perceptible jaundice.

Read before the Society for Pediatric Research, May 5, 1936.

From the New York Hospital and the Department of Pediatrics, Cornell University Medical College.

1. Boyd, E. M.: A Differential Lipid Analysis of Blood Plasma in Normal Young Women by Micro-Oxidative Methods, J. Biol. Chem. **101**:323, 1933; The Lipid Content of the White Blood Cells in Normal Young Women, ibid. **101**:623, 1933.

2. Kirk, E.; Page, I. H., and Van Slyke, D. D.: Gasometric Microdetermination of Lipids in Plasma, Blood Cells, and Tissues, J. Biol. Chem. **106**:203, 1934.

3. Sperry, W. M.: Cholesterol of the Blood Plasma in the Neonatal Period, Am. J. Dis. Child. **51**:84 (Jan.) 1936.

METHODS

Analyses were made of 10 cc. samples of blood withdrawn from the internal jugular vein. The blood was immediately placed in a dry bottle containing 4 mg. of heparin, shaken by revolving the receptacle a few times, transferred to a dry graduated centrifuge tube and centrifugated for forty-five minutes at 2,500 revolutions per minute. A hematocrit reading was then made and the icteric index determined; the plasma and cells were separated, and their lipid fractions were measured. Only the results for the plasma lipids are considered in this communication.

By use of the gasometric micromethods of Kirk, Page and Van Slyke,[2] analyses of the several lipid fractions were possible with small amounts (3 cc.) of plasma. The total lipids (as lipid carbon), total and free cholesterol and lipid phosphorus were directly measured, and from these values the neutral fat, cholesterol ester and phosphatide fractions were calculated for each specimen. Analyses were made in duplicate; the average percentages of error of the duplicates were 1.7 for total lipid carbon and 1.8 for total cholesterol and free cholesterol in the day old and week old groups, whereas the error was 14 per cent for lipid phosphorus in the day old series and 4.5 per cent for the week old group. These deviations exceed those reported by Kirk, Page and Van Slyke[2] and are probably explained by the presence of smaller amounts of the various lipid constituents, especially phosphorus, in the plasma of new-born infants. The reproducibility of the method was determined by analyses of known solutions and their recovery when added to stock plasma. Analysis of a known amount of a solution of cholesterol palmitate resulted in 105 per cent recovery, with 95 per cent of this regained when added to plasma. From a solution of purified cholesterol (melting point 148.5) a 92 per cent recovery was obtained on analysis, with 99.3 per cent of this recovered when added to plasma. Determination of lipid phosphorus in a solution of egg lecithin gave 102 per cent of the calculated amount and a recovery of 94 per cent when added to plasma.

CALCULATION

From the directly determined fractions the following calculated data were obtained, the factors and formulas of Page and his associates[4] being used.

Phosphatides = lipid phosphorus × 23.5
Esterified cholesterol = total cholesterol — free cholesterol
Cholesterol esters = esterified cholesterol × 1.69
Neutral fat = neutral fat carbon × 1.32

The neutral fat carbon was determined by obtaining the difference between total lipid carbon and the sum of lipid phosphorus carbon and free and esterified cholesterol carbon; with the introduction of the factors used in the calculation of the latter constituents, this can be formulated as follows:

Neutral fat carbon = total lipid carbon — [(lipid phosphorus × 15.5) + (free cholesterol × 0.839) + (esterified cholesterol × 1.40)].

The material designated neutral fat probably contains some unidentified extractive soluble in purified petroleum benzine.

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4. Page, I. H.; Kirk, E.; Lewis, W. H., Jr.: Thompson, W. R., and Van Slyke, D. D.: Plasma Lipids of Normal Men at Different Ages, J. Biol. Chem. **111**:613, 1935.

Total lipids = phosphatides + free cholesterol + cholesterol esters + neutral fat.

Values for total lipids were also calculated, by multiplying the total lipid carbon by the factor 1.3, as suggested by Page and his associates. The average difference between the figures obtained by the two methods was 2.7 per cent on the day of birth and 1.5 per cent for the week old group.

STATISTICAL ANALYSIS

The mean value for each lipid was determined, and from it the standard deviation and probable error were calculated by the formulas

$s = \sqrt{\Sigma(x)^2/n}$ and P.E. $= 0.6745\ (s/\sqrt{n})$, in which s indicates the standard deviation, Σ is a summation symbol, x indicates the variation of each value from the mean and n indicates the number of analyses.[5]

The only data rejected were those for case 25. The values for total lipid carbon and lipid phosphorus deviated so much from those obtained in the other twenty-four cases that it seemed preferable to exclude them in the calculation of "normal" means and range.

RESULTS

The protocols of the infants and detailed chemical data are given in table 1. In table 2 the means, standard deviations and ranges of the values for total plasma lipids and for the individual lipid components are collected and compared with the figures reported for adults.[4] Although the values for total content and individual lipids show rather wide fluctuations in each age group, those for all the lipid components show a definite tendency to rise with increasing age. That this rise is significant is evident from the statistical comparison of the means in table 2, the difference between the means being three and one-half times or more greater than the probable error of the difference in every instance.

Because of the variability of the individual lipid constituents, it was decided to compare these with the magnitude of variability of the ratios between the different constituents. Only one ratio (esterified to total cholesterol or, conversely, free to total cholesterol) was found to show a greater constancy than the individual components used in its calculation. The ratios of esterified to total cholesterol on the first day of life varied between 0.51 and 0.68, with a mean of 0.60 ± 0.05; the coefficient of variability within this group was only 8 per cent, while the individual coefficients of variability of the figures for esterified and total cholesterol used in their calculation were 23 per cent and 18 per cent, respectively. From the sixth to the tenth day of life the limits of this ratio were between 0.53 and 0.69, with a mean of 0.62 ± 0.04, the average deviation of this group being 6 per cent, as against 17 and 14 per cent for esterified and total cholesterol, respectively.

5. Dunn, H. L.: Application of Statistical Methods in Physiology, Physiol. Rev. **9**:275, 1929.

TABLE 1.—*Blood Plasma Lipids in Normal New-Born Infants (in Milligrams per Hundred Cubic Centimeters)*

Case	Sex	Age	Directly Determined		Cholesterol				Calculated			Number of Hours Fast	Feeding
			Total Lipid Carbon	Total Lipid Phosphorus	Total	Free	Esterified	Esters	Phosphatides	Neutral Fats	Total Lipids		
1	F	5¾ hr.	157	1.0	120	44	76	128	24	8*	204*		
		9 days	345	2.3	167	63	104	176	54	146	439	3½	Breast
2	M	10 hr.	150	0.7	55	27	28	47	16	102	192		
		8 days	331	5.5	130	43	87	147	129	116	435	3¾	Breast
3	F	8 hr.	158	0.8	57	23	34	57	19	104	203		
		8 days	337	4.6	109	48	61	103	108	185	444	3¾	Breast
		7 days	310	4.7	120	37	83	140	110	119	406	8	
4	M	8 hr.	159	1.8	65	31	34	57	42	76	206		
		8 days	461	6.5	132	49	83	140	153	268	610	4	Cow's milk formula
5	F	5¾ hr.	175	1.4	89	31	58	98	33	61	223		
		8 days	493	8.1	179	68	111	188	190	295	651	4	Breast
6	M	6 hr.	251	4.0	91	37	54	91	94	109	331		
		9 days	473	7.3	136	57	79	134	172	266	629	4	Breast
		7 days	397	6.7	147	51	96	162	157	153	523	11½	
7	M	6½ hr.	196	2.6	74	32	42	71	61	92	256		
		9 days	361	5.1	115	48	67	113	120	195	476	4	Breast
		7 days	239	1.6	108	41	67	113	38	114	306	11	
8	M	12¾ hr.	150	0.3	93	35	58	98	7	46	186		
		6 days	364	6.5	133	51	82	139	153	139	482	5	Cow's milk formula
9	M	5½ hr.	105	0.5	76	32	44	74	12	12	130		
		7 days	312	3.9	127	43	84	142	92	129	406	5	Breast
10	M	3 hr.	179	1.6	78	28	50	85	38	80	231		
		7 days	421	4.3	128	48	80	135	101	267	551	5	Breast
11	F	3 hr.	116	0.2	86	31	55	93	5	13	142		
		7 days	391	5.3	134	49	85	144	125	196	514	5	Breast

12	M	5 hr. 7 days	112 276	0.2 2.1	67 129	27 48	40 81	68 137	5 49	40 119	140 353	5¾	Breast
13	M	1 hr. 7 days	198 407	2.3 4.3	69 119	30 50	39 69	66 117	54 101	109 266	259 534	6	Breast
14	F	5 hr. 8 days	227 464	2.3 7.2	78 155	32 57	46 98	78 166	54 169	132 221	296 613	6	Breast
15	F	4 hr. 9 days	179 366	0.8 4.1	72 147	34 59	38 88	64 149	19 96	112 171	229 475	8	Breast
16	M	7 hr. 8 days	199 317	1.6 4.1	86 120	40 57	46 63	78 106	38 96	101 155	257 414	8	Breast
17	M	6½ hr. 8 days	155 240	0 0.9	90 128	30 41	60 87	101 147	0 21	60 92	191 301	8	Breast and cow's milk formula
18	F	4½ hr. 9 days	231 370	1.0 2.6	88 140	37 51	51 89	86 150	24 61	149 214	296 476	8	Breast and cow's milk formula
19	M	5 hr. 10 days	127 355	0.5 4.3	67 117	29 51	38 66	64 112	12 101	55 202	160 466	8	Breast
20	F	3 hr. 10 days	148 303	0 1.1	102 174	39 62	63 112	106 189	0 26	36 102	181 379	8	Breast
21	F	7 hr. 7 days	231 400	0.7 5.2	88 151	28 55	60 96	101 162	16 122	149 183	294 522	11	Breast
22	M	7 hr. 7 days	98 236	0 0.8	73 122	24 45	49 77	83 130	0 19	12 103	119 297	11	Breast
23	M	5 hr.	211	1.4	74	31	43	82	33	136	282		
24	F	5 hr.	222	1.9	79	29	50	95	45	130	299		
25†	M	4 hr. 8 days	476 367	5.6 5.2	117 142	39 53	78 89	132 150	132 122	326 157	629 480	11	Breast

* Calculated using equation: total lipid = 1.3 (total lipid carbon).
† Omitted from all calculations.

TABLE 2.—*Mean Plasma Lipids in New-Born and in Adults (in Milligrams per Hundred Cubic Centimeters)*

Number of Subjects	Sex	Age	Directly Determined						Calculated		
			Total Lipid Carbon	Total Lipid Phosphorus	Cholesterol				Phosphatides	Neutral Fats	Total Lipids
					Total	Free	Esterified	Esters			
			Range								
24	14 M 10 F	1-13 hr.	98 - 251	0 - 4.0	55 - 120	23 - 44	28 - 76	47 - 128	0 - 94	8 - 149	119 - 331
25	15 M 10 F	6-10 days	236 - 493	0.8 - 8.1	108 - 179	37 - 68	61 - 112	103 - 189	19 - 190	92 - 268	297 - 651
66 [4]	M	20-91 yr.	350 - 970	2.6 - 14.2	118 - 360	56 - 121	51 - 261	86 - 440	60 - 335	50 - 580	450 - 1260
			Mean ± Standard Deviation								
24	14 M 10 F	1-13 hr.	172 ± 43	1.2 ± 0.97	80 ± 14	32 ± 5	48 ± 11	82 ± 18	27 ± 23	80 ± 44	221 ± 60
25	15 M 10 F	6-10 days	359 ± 71	4.4 ± 2.1	135 ± 19	51 ± 7	84 ± 14	142 ± 23	103 ± 48	173 ± 55	468 ± 98
66 [4]	M	20-91 yr.	566 ± 166	7.7 ± 3.0	232 ± 62	82 ± 17	146 ± 56	247 ± 95	181 ± 71	225 ± 137	735 ± 216
			Difference Between Means ± Probable Error of Difference								
24	14 M 10 F	1-13 hr.	187 ± 12	3.2 ± 0.3	55 ± 4	19 ± 1.4	36 ± 3	60 ± 4	76 ± 7	93 ± 9	247 ± 15
25	15 M 10 F	6-10 days									
25	15 M 10 F	6-10 days	207 ± 17	3.3 ± 0.7	97 ± 6	31 ± 1.4	62 ± 5	105 ± 9	78 ± 9	52 ± 14	267 ± 22
66*	M	20-91 yr.									

* The values used here were calculated from the data of Page and his associates.

The variability in general of the ratios of one lipid to another in these infants in contrast to their usual constancy in adults cannot be explained. The significance of the constancy of the ratio of esterified to total cholesterol and its persistence from the early part to the end of the neonatal period is also not clear. The usefulness of these ratios will become apparent only when more of them are computed for older infants, healthy and sick.

The percentage composition of the plasma lipid mixtures are recorded in table 3 and compared with the figures for adults collected by Page and his associates.[4]

In terms of percentages of the total, the phosphatide concentration increased with age, while the cholesterol ester and free cholesterol fractions diminished. The percentage composition of the plasma lipids at

TABLE 3.—*Percentage Composition of Plasma Lipid Mixtures in New-Born and in Adults*

Age	Phosphatides Mean ± P. E.* Percentage	Free Cholesterol Mean ± P. E.* Percentage	Cholesterol Esters Mean ± P. E.* Percentage	Neutral Fats Mean ± P. E.* Percentage
1 to 13 hours	11.0 ± 1.0	15.0 ± 0.6	40.0 ± 2.0	34.0 ± 2.0
6 to 10 days	21.0 ± 1.0	11.0 ± 0.3	32.0 ± 1.1	36.0 ± 0.9
20 to 91 years [4]	23.6 ± 0.5†	11.8 ± 0.3	35.4 ± 0.9	28.2 ± 1.0
	Differences of Means ± Probable Error of Difference			
1 day to 1 week	10.0 ± 1.5	4.0 ± 0.7	8.0 ± 2.3	2.0 ± 2.2
1 week to adult	2.6 ± 1.1	0.8 ± 0.4	3.4 ± 1.4	7.8 ± 1.3

* Probable error of mean.
† Calculated from data given by Page and his associates.[4]

the end of the neonatal period approximated the reported lipid constitution of adults except in concentration of neutral fat, the plasma of the new-born containing an appreciably greater amount of this fraction.

COMMENT

The data presented in this paper demonstrate that all the lipid constituents of the blood plasma tend to increase from birth to the end of the neonatal period but that the level at the end of that period is appreciably lower than that during adult life. The factors responsible for the changes in the plasma lipids within the first two weeks of life cannot readily be identified. The initial level of the plasma lipids at birth is probably dependent on the amounts of lipid passing through the placenta and the absorptive power of the tissues of the fetus at the time of delivery and shortly thereafter. It has often been shown that the blood of pregnant women at term has a high lipid content. That some of this passes through the placenta to the fetus has been demonstrated by Boyd,[6] who showed that phospholipid and free cholesterol

6. Boyd, E. M., and Wilson, K. M.: The Exchange of Lipids in the Umbilical Circulation at Birth, J. Clin. Investigation **14**:7, 1935.

are regularly absorbed by the human fetus from the umbilical blood and that cholesterol esters and neutral fat may be absorbed if present in sufficient quantities. In this study no relationship was apparent between the weight and the sex of the infant or anesthesia of the mother and the quantity of the lipids on the first day of life; some of the lightest babies had the highest lipid levels.

The augmentation in the amounts by the end of the neonatal period was probably a true increase and not the result of extraneous factors, such as dehydration or severe icterus. The second determination of the lipid content of the blood of each infant was made between the sixth and the tenth day, when the infants were regaining their birth weights and were in comparable states of nutrition and when the clinical appearance, hematocrit estimations and icteric indexes showed these factors to be absent. Furthermore, repeated observations on two of the infants (table 1, cases 8 and 9) at the age of 6 weeks yielded progressively increasing values for lipids, lending support to the belief that the rise is continuous during early infancy, when the aforementioned extraneous factors may be excluded with certainty. The total lipid carbon rose from 364 to 550 mg. in case 8 and from 312 to 400 mg. in case 9.

Other extraneous factors which are known to influence the plasma lipid levels are the type of meal ingested and the interval following the last meal, which varied between three and one-half and eleven hours in these observations. Our data do not permit proper evaluation of the effect of the first of these, since all but two of the twenty-five babies received breast milk every four hours for five feedings, two received a complementary cow's milk formula six times daily and two received cow's milk alone. In regard to the second factor, segregation of the results for the fourteen infants after a short fast (from three and one-half to six hours) from those of the eleven infants after a long fast (eight to eleven hours) revealed that the former had somewhat greater total lipid, neutral fat and lipid phosphorus contents than the latter, with no difference in cholesterol values. The means, with the probable errors of their differences, were as follows, the larger figures representing the group which had a short fast: for total lipid carbon, 388 mg. and 321 mg., with a difference of 67 ± 16.7; for lipid phosphorus, 5.2 mg. and 3.3 mg., with a difference of 1.9 ± 0.5, and for neutral fat, 194 mg. and 146 mg., with a difference of 48 ± 13. It is conceivable that if a larger series of infants with a long period of fasting had been studied, somewhat lower mean values than those reported here for the end of the neonatal period might have been obtained. However, despite the significant differences revealed in the analysis, the fact remains that the figures obtained from the sixth to the tenth day of life after pro-

longed fasting (from eight to eleven hours) remained appreciably higher than those on the day of birth.

The disparity of values for plasma lipids between the neonatal period and adult life has not previously been sufficiently emphasized. Further studies are under way to determine the normal ranges and means at other periods in infancy and to ascertain the period during childhood when these measurements approach those of the adult levels. It is obvious that such standards must be established before significance is ascribed to deviations obtained from measurements on the plasma of sick infants and children.

SUMMARY

The plasma lipids of twenty-five normal new-born babies were measured on the day of birth and again from the sixth to the tenth day of life to serve as a basis of comparison for similar studies of pathologic states. The range of each lipid and its mean and standard deviation were established.

The range of values for each lipid constituent was shown to vary widely, but the amounts of both the total lipids and their fractions rose significantly with increasing age during the neonatal period; the mean levels attained by the older infants in this group remained appreciably lower than those reported for adults when measurements were made by the same chemical procedures.

Analyses of the ratios of one lipid constituent to another showed constancy only in that of esterified to total cholesterol (conversely, free to total).

The percentage composition of the plasma lipid mixture of infants aged from 6 to 10 days approximated that of the adult, except that the neutral fat fraction for the infants was larger.

The lability of the plasma lipid levels during the neonatal period may be related to the general instability of the rapidly changing organism during the first two weeks of life.

DISCUSSION

DR. C. F. MCKHANN, Boston: Dr. Sperry, would you like to open the discussion?

DR. W. M. SPERRY, New York: I was particularly interested in the relation between Dr. Senn's results and my own, to which he referred, in regard to the proportion between the different cholesterol fractions. My study was limited entirely to cholesterol. The essential finding in my investigation, which I may have an opportunity to comment on later today, was that the proportion is much more variable in the first few days of life and, expressed as the percentage of free cholesterol to the total cholesterol content, is considerably higher, on the average, than is the case in adults. However, there appears to be a trend toward the adult level with an increase in age up to 25 days. I should like to ask Dr. Senn whether any such observations were made and whether his results are in accord with this finding.

I found a rather sharp increase in the concentration of total cholesterol during approximately the first four days of life in a number of subjects in whom two or more analyses, covering different intervals of time, were done. I should like to ask whether Dr. Senn observed such increases.

I congratulate Dr. Senn on his investigation because he has presented data which have not, so far as I know, hitherto been available.

Dr. M. J. E. Senn, New York: From further study of 2 of the infants at the age of 6 weeks it is apparent that the total cholesterol content and the other fat fractions continue to increase with age, as Dr. Sperry has mentioned. We believe that this is a true increase, because at the age of 6 weeks the factors of jaundice and dehydration were not apparent. The values for the fats were definitely greater than the limits which we gave during the period directly after birth.

As to the constancy of the ratios of one fat fraction to another, it is possible that they become more constant with increasing age. We do not have figures to prove that point.

HEREDOFAMILIAL DEVIATIONS

I. THE LAURENCE-MOON-BIEDL SYNDROME

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AND

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CINCINNATI

Hereditary deviations seldom appear singly. Owing to the variety of their combinations, each observer, influenced by his special interest in some particular phase of medicine as well as by chance, encounters certain sets of symptoms more frequently than others. After seeing several instances of a particular combination of symptoms, he may arrive at the conclusion that he has discovered a definite disease entity, which he describes as such. Thus the literature contains contributions which, valuable though they may be, often result in special emphasis on one combination of symptoms to the neglect of others. This leads to speculations on the etiology of the syndrome which cannot be substantiated when other cases with different combinations of symptoms are taken into consideration.

No doubt certain syndromes do occur more frequently than others, but there are always so many transitional forms that the exceptions abrogate the rule and an exact demarcation of the syndromes appears hopeless. This fact, which was stressed in 1897 by Jendrássik in an article on hereditary diseases of the central nervous system, certainly holds true for all other forms of hereditary disease.

Recently a symptom complex consisting of obesity, hypogenitalism, retinitis pigmentosa, mental deficiency and polydactylism has been described in the pediatric literature under the name of the Laurence-Moon-Biedl syndrome. By analysis of several related cases and by a survey of the literature on the subject, an attempt will be made to show that this syndrome does not represent a disease entity but is a rare combination of more or less frequent heredofamilial symptoms.

REPORT OF CASES

CASE 1.—J. L. (fig. 1), a colored boy 16 years of age, entered the Children's Hospital in January 1936 because of his deformities and backwardness in school.

History.—According to the statement of the boy's guardian, no other member of the family had webbed or extra fingers or toes, blindness, deafness or mental

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abnormality. This history is, however, not necessarily reliable, and no information was obtained concerning the type of the patient's birth or his development. One uncle was fat; another had been committed to an institution for a sexual offense. The mentality of two young cousins was considered to be above the average. There was no history of illness, accident or operation.

Examination.—The measurements were as follows:

	J. L.	Average
Height	161 cm.	160 cm.
Upper measurement	75 cm.	79 cm.
Lower measurement	86 cm.	81 cm.
Span	160 cm.	165 cm.
Circumference of the head	56 cm.	55 cm.
Circumference of the chest	106 cm.	79 cm.
Circumference of the waist	102 cm.	102 cm.
Weight	198 lb. (89.8 Kg.)	109 lb. (49.4 Kg.)

There was obesity of Fröhlich's type, with marked development of fat in the mammary region, abdomen, gluteal region and thighs. Perspiration was frequent and profuse. The nipples were inverted. The development and distribution of the hair were normal for the patient's age. The eyebrows curved upward.

The skull was typically acrocephalic, with the greatest height in the region of the closed anterior fontanel. The line from the occiput to the neck was almost straight. When viewed from the side the frontal bone appeared to be concave, and there was no depression at the root of the nose. The facial diameter from one malar bone to the other was 17.5 cm. At the height of the forehead the diameter was 12.5 cm., and the width decreased to the top of the head, giving the boy the peculiar aspect seen in figure 1.

The distance between the inner angles of the protruding eyes was abnormally wide (hypertelorism), and a distinct epicanthic fold was present. The palpebral fissures appeared normal. The extra-ocular movements were normal. The cornea was shiny, transparent and smooth. The irises were brownish, enclosing round and equal pupils that reacted normally to light and in accommodation. The fundi and ocular fields were normal.

The ears were relatively small and the lobes poorly developed. Above the lobe on each side was a groove apparently corresponding to a branchial fistula. There was no groove between the helix and the antitragus. The landmarks were distinct on the tympanic membrane, and the hearing was normal.

The lips were thick. The upper incisors were far apart. In the upper jaw the canines were just appearing; in the lower jaw the left canine was present, but only the point of the right was visible. The tongue was large but had no transverse fissures and was not protruding. The hard palate was arched; the chin receded. The angle between the body and the ramus ascendans of the mandible was wide. There was a deep depression at the insertion of the masseter muscle.

The neck was thick, being 48 cm. in circumference. The thyroid gland was not palpable. The thorax was barrel shaped. Examination of the chest, heart and abdomen revealed nothing abnormal. The systolic blood pressure was 145 and the diastolic 100.

The penis was normal, but the scrotal fold could hardly be seen and the testicles could not be palpated.

When the boy was standing, his trunk was bent forward and his upper extremities reached halfway down his thighs. The upper arm was fat. There was no deformity at the elbow, and movement was complete. The hands were short.

There was complete syndactylism of the third, fourth and fifth fingers of the left hand. The right hand showed incomplete syndactylism throughout. The fingers were short and broad. The third, fourth and fifth fingers of the left hand and the third and fourth fingers of the right could not be extended.

The thighs were extremely fat and heavy. This was probably due to the bony structure, since the distance between the internal and the external epicondyle was about 16 cm. The patella of the left knee was displaced laterally. The feet were short, and there were six toes on each foot. There was complete syndactylism of all the toes except the sixth. There was pronounced genu valgum, and the boy walked slowly and with difficulty. The gait was peculiar in that one knee was placed in front of the other.

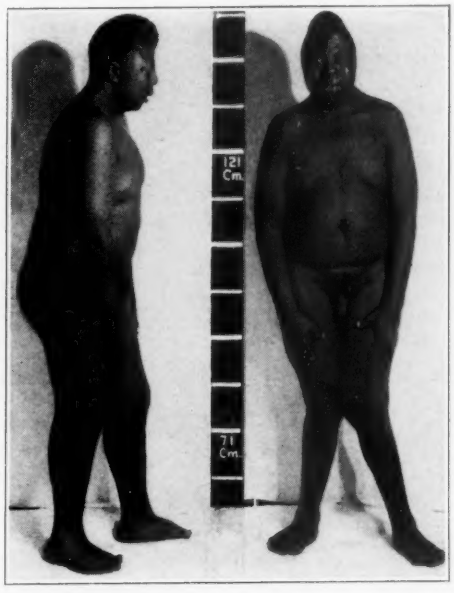

Fig. 1.—Photographs of J. L., showing the acrocephalosyndactylism, polydactylism, obesity and genu valgum.

The neurologic examination gave negative results.

An exact mental test was not done on the patient during his short stay in the hospital. It was reported that when he was 14 years of age his intelligence quotient had been 60. He was able to talk and had learned to read, but he reacted in a childish manner to his surroundings and cried easily. He was, however, able to run errands and do chores about the house. Altogether he gave the general impression of having the mental age of about 7 years.

The laboratory findings were as follows: The urine was normal. Examination of the blood showed no anemia and no abnormality of the cells. A Kahn test of the blood was negative. The tuberculin reaction was positive. The basal metabolic rate was — 1 per cent.

On the patient's first visit to the hospital, at the age of 11 years, the roentgenographic examination had revealed the following conditions: In the right and left hands there was an extra center of ossification, with abnormal development and

imperfect fusion of the fragments involving the proximal phalanx of the thumb. Development of the epiphysis of the proximal phalanx of the index finger was abnormal. The second and fifth fingers showed two phalanges only. Between the proximal and the distal phalanx of the third and fourth fingers were some small round centers of ossification, which probably represented the middle phalanges. In the wrist all the centers of ossification, including the pisiform, were present and of adequate size. In both feet there was a developmental deformity of the proximal phalanx of the first toe and an extra fragment on the mesial side of the distal end of the metatarsal bone of the second toe. There were six toes on each foot. Some flattening of the distal portion of the distal phalanx of the second and third toes was found. The basal phalanx of the first toe consisted of two equal parts. The rest of the toes showed two phalanges only. On the mesial side of the carpo-

Fig. 2.—Roentgenograph of the skull of J. L.

metacarpal joint of the second toe a globular center of ossification was visible. The shaft of the right femur was curved and thickened, but there was no other gross change of the long bones.

In the stereoscopic roentgenogram, the skull had been seen to be deformed in its various diameters.

In 1936, when the patient was 16 years of age, roentgenographic examination showed that the left patella was on the outer side of the femur and that the tibia was displaced outward and backward. The cervical, dorsal and lateral lumbar sections of the spine were curved forward, and there was a lateral curve in the upper dorsal region. Otherwise the findings were the same as those reported five years before (figs. 2 and 3).

Acrocephaly, polydactylism, syndactylism, mental deficiency, obesity and genital dystrophy were the most striking features in this case.

The combination of the first two symptoms is the well known syndrome called by Apert acrocephalosyndactylism; the polydactylism or syndactylism, obesity, mental deficiency and genital dystrophy might be considered an incomplete Laurence-Moon-Biedl syndrome, incomplete because retinitis pigmentosa was not present. A condition with a striking resemblance to the one just described was reported on by Turner as a Laurence-Moon-Biedl syndrome. The resemblance of the two syndromes extends not only to the "turret head," the syndactylism, the polydactylism, the mental deficiency, the genital dystrophy and the normal condition of the eyegrounds, but also to the genu valgum, the displacement of the patella, the deformities of the thumbs and the middle phalanges, as seen in the roentgenograms, and the delay

Fig. 3.—Roentgenogram of the hand and of the foot of J. L.

in the eruption of some of the teeth. "Tempting as it would be to introduce into pathology the syndrome observed by us under the name of a new form of disease, we refrain from it, since among the group enumerated here there are still differences, and the syndromes could be increased infinitely." This sentence, taken from Jendrássik's previously cited article, can be applied here as well as in all other discussions of heredofamilial syndromes.

The next group of patients consists of 3 siblings, to the reports of whose cases is added certain information about the family history.

Family History.—The maternal grandfather had syndactylism. The succeeding generation was apparently free from deformities, but 4 grandchildren, including 1 of the children described, had syndactylism.

The father was 44 years of age, was in good health and had no deformity. The mother was 40 years of age and had had no serious illness until 1932, when minimal pulmonary tuberculosis developed, from which she apparently recovered. She was talkative and excitable and appeared to enjoy exhibiting the defective daughter.

Three premature children had been born in succession: The first, born at 5 months, lived an hour and a half; the second, born at 8 months, lived twenty-four hours, and the third, born at 6 months, lived twelve days. No deformity was found. The fourth child was born at full term and was well formed but died at the age of 2 years of bronchopneumonia as a complication of pertussis. The oldest living sibling was a boy (Sherman H.); the next child, a girl (Shirley H.), and the youngest, a boy (J. H.). The seventh pregnancy resulted in a 7 month premature child. A Kahn test of the mother's blood was negative.

CASE 2.—*History.*—Shirley H., a girl aged 11 years (fig. 4), had been a full term baby with an uncomplicated delivery. Her weight at birth had been 6 pounds (2,721 Gm.). The eruption of the teeth and the ability to sit up, to walk and to talk had been normal. She had had measles and chickenpox at 5 and at 8 years,

Fig. 4.—Shirley H.

respectively, without complications. There had been no other illness and no accident or operation.

The patient was brought to the Children's Hospital because of blindness and headache. The blindness was said to have been first noticed at the age of 17 months. When 4 years of age she had been seen at the Massachusetts Eye and Ear Infirmary, Boston, and the examination at that time showed the following condition: Her eyes diverged when at rest but showed good excursions. The pupils were dilated and reacted in accommodation but not to light. The tension was normal to palpation, and the media were clear. With the patient under ether anesthesia the nerve heads and fundi appeared normal. The neurologic examination gave negative results.

The girl complained of intermittent attacks of dull and steady occipital pain, which sometimes lasted twenty-four hours. She could perceive light.

At 5 years of age, after a stay of ten months, she had been dismissed from the Perkins Institute for the Blind, Columbus, Ohio, because of behavior difficulties.

When she was there her intelligence quotient had been rated at 70 on one occasion and at 80 on another. At 9 years of age her intelligence quotient had been rated as 56 and her mental age as 6 years according to the Hayes Revision of the Binet scale at the Psychological Laboratory, Cincinnati.

Examination.—Her measurements were as follows:

	Shirley H.	Average
Height	133 cm.	141 cm.
Upper measurement	64 cm.	71 cm.
Lower measurement	69 cm.	71 cm.
Span	133 cm.	141 cm.
Circumference of the head	51 cm.	52 cm.
Circumference of the chest	63 cm.	67 cm.
Circumference of the waist	58 cm.	57 cm.
Weight	65 lb. (29.5 Kg.)	76 lb. (34.5 Kg.)

The patient was poorly nourished and poorly developed. She walked with a normal gait. The skin was smooth and of normal texture. There was an abundant growth of fine, dark brown hair on the head. The eyelashes were long. There was an extensive growth of hair on the arms but none in the axillary region. The pubic hair was beginning to develop. The development and distribution of the adipose tissue were normal. The head was dolichocephalic, with a low forehead.

The eyes showed nystagmoid, searching movements. The conjunctivae and scleras were normal. The irises were grayish blue. The pupils were semidilated and sluggish to light and in accommodation. The corneas appeared larger than normal and were conical, as in keratoglobus. The right lens showed a posterior cortical spicular opacity in one portion. The vitreous on the right showed a few "floaters." The pigment in the retinas of the entire periphery showed typical "bone-corpuscle"-shaped degeneration. There was pigment in the macular region, and there was secondary atrophy of the optic nerve. The left eye showed the same picture as the right except that the macula had been spared. Perception of light was present, but the patient was unable to count fingers at a distance of 1 foot (33 cm.).

Externally the mouth was characterized by protrusion of the front teeth of the upper jaw. There was a gap between the two medial incisors of the upper jaw and a larger one between the medial and the lateral incisor. The incisors of the lower jaw appeared normal. The ears were of normal size and form. The thyroid gland was slightly palpable. The development of the breasts was slight. Examination of the heart, lungs and abdomen revealed nothing abnormal. The external genitalia were those of the average preadolescent girl of the patient's age. There was bilateral syndactylism of the second and third toes and of the third and fourth fingers. There was bilateral pes planus. The reflexes were normal, and there was no paralysis.

The urine was normal. Examination of the blood revealed moderate anemia; the red blood cells were diminished in number but showed no other abnormality. The Kahn and the Wassermann reaction of the blood were negative, as was the reaction to tuberculin. The basal metabolic rate was +1.1 per cent. The sugar content of the blood during fasting was 80 mg. per hundred cubic centimeters; the cholesterol content of the whole blood, 189 mg.; the cholesterol content of the plasma, 213 mg.; the calcium content, 11 mg., and the phosphorus content, 5.1 mg.

Roentgenograms of the skull showed that the bones were normal. The sella turcica was of normal size. There was a flattening at the terminal end of the distal phalanges of the second toes of both feet and to a lesser extent of the third toes.

CASE 3.—*History.*—Sherman H., a boy of 13 years (fig. 5), had been a full-term baby, and the delivery had been uncomplicated. The weight at birth had been 7½ pounds (3,402 Gm.). Apparently the boy had developed normally. He had had measles and chickenpox at the ages of 5 and 7 years, respectively, with no complications. There had been no other illness and no accident or operation.

The child was brought to the Children's Hospital on Dec. 22, 1935, with the complaint of persistent boils for the preceding two months and mild "deafness." The deafness was promptly relieved by removal of half of a small rubber eraser from each external auditory canal, together with inspissated wax. The boils rapidly improved under symptomatic treatment. The child had always been smaller than the average boy of his age, but the mother had attached no significance to this anomaly.

Fig. 5.—Sherman H., brother of Shirley H.

Examination.—His measurements were as follows:

	Sherman H.	Average
Height	129 cm.	150 cm.
Upper measurement	63 cm.	74 cm.
Lower measurement	66 cm.	76 cm.
Span	131 cm.	153 cm.
Circumference of the head	55 cm.	53 cm.
Circumference of the chest	64 cm.	71 cm.
Circumference of the waist	64 cm.	63 cm.
Weight	62 lb. (28.1 Kg.)	89 lb. (40.4 Kg.)

All the measurements were smaller than the average, but the proportions were normal.

The skin was rough and dry and had a grayish tint, particularly over the extremities. The hair on the head was medium brown and abundant. The eyelashes were long. The growth in the axillary and pubic regions was scanty. The skull was dolichocephalic. The irises were gray, enclosing round pupils that reacted normally to light and in accommodation. The extra-ocular movements were normal. The fundi were normal. The teeth were well alined. The tongue was of normal size, and no fissures were present. Several nasolabial folds on each side of the mouth gave the boy an appearance of being older than he was. The neck was short. Examination of the lungs and heart revealed nothing abnormal. The genitalia were normal. There were lordosis of the lumbar portion of the spine and incurving of the little fingers.

The urine was normal, and examination of the blood showed only moderate anemia. The reaction to tuberculin and the Kahn and the Wassermann reaction of the blood were negative. The basal metabolic rate was —10 per cent. The sugar content of the blood during fasting was 124.2 mg. per hundred cubic centimeters; the cholesterol content of the whole blood, 181 mg., and the cholesterol content of the plasma, 173 mg.

Roentgenograms of the skull showed no evidence of disease of the bones. The sella turcica appeared to be slightly smaller than normal. The wrists were normal. The terminal phalanges of the fingers were blunt but were otherwise normal.

The intelligence quotient was 93.

CASE 4.—*History.*—J. H., a boy aged 9 years (fig. 6), had been a full term baby; the delivery had been uncomplicated. The weight at birth had been 8½ pounds (3,855 Gm.). Development had apparently been normal. The boy had had chickenpox, measles and whooping cough at the ages of 5, 6 and 7 years, respectively, with no complications. At 6 years of age primary pulmonary tuberculosis developed. He recovered and since then has had no other illness and no accident or operation and has appeared to be in good health.

This boy had always been small but otherwise had had no abnormal condition. At the age of 6 he weighed 30 pounds and his height was 94 cm.

Examination.—His measurements were as follows:

	J. H.		Average	
Height	113 cm.		131 cm.	
Upper measurements	57 cm.		66 cm.	
Lower measurements	56 cm.		65 cm.	
Span	111 cm.		131 cm.	
Head circumference	52 cm.			
Chest circumference	52 cm.		63 cm.	
Waist circumference	52 cm.		56 cm.	
Weight	44 lb.	(20 Kg.)	62 lb.	(28.1 Kg.)

The boy had normal proportions but was small in all measurements. His height was 18 cm. shorter than the average for his age.

The skin was roughened and dry, particularly over the extremities. There were several small pigmented nevi on the shoulders. The hair on the head was blond, fine and abundant. The eyelashes were long. Pubic and axillary hair was absent. There was a moderate growth of hair on the back and a marked growth on the extensor surfaces of the forearms. The skull was dolichocephalic, and the forehead was low. The eyes protruded slightly. The upper half of the

left iris was brown, and the lower half, gray. The iris of the right eye was gray. The right pupil measured 5 mm., and the left, 3 mm. The left pupil reacted better to light and in accommodation than the right. The conjunctivae, scleras, corneas, lenses and media were normal. The fundi were normal except for several streaks in the choroid in the upper and outer parts of the right uvea, which were interpreted as evidence of healed focal choroiditis. The ears were normal. The teeth were normal in position, and there was moderate dental caries. Several nasolabial folds on each side of the mouth gave the boy an appearance of being older than he was. The neck was short, and the thyroid gland was not palpable. Examination of the chest, heart and abdomen revealed nothing abnormal. The genitals were normal for the age. The spine showed marked lordosis in the lumbar portion. The extremities were normal.

Fig. 6.—J. H., brother of Shirley H.

The urine and the blood were normal. The Kahn and the Wassermann reaction of the blood were negative. The reaction to tuberculin was positive. The basal metabolic rate was + 8 per cent. The sugar content of the blood during fasting was 94 mg. per hundred cubic centimeters; the cholesterol content of the whole blood, 179 mg., and the cholesterol content of the plasma, 194 mg.

Roentgenograms of the skull showed normal development of the bones, but the sella turcica appeared to be smaller than normal. Ossification of the carpal bones of the wrists had not been delayed.

According to the Stanford-Binet test the patient's mental age was 10 years and 4 months (actual age, 9 years and 9 months) and his intelligence quotient 106. He was treated with an extract of the anterior lobe of the pituitary gland,[1] receiving from 2 to 5 cc. twice a week for two months, without appreciable effect.

1. The preparation used was antuitrin G.

The combination of retinitis pigmentosa, mental retardation and syndactylism in the girl (case 2), the occurrence of dwarfism in the 2 brothers (cases 3 and 4) and the history of syndactylism in the grandfather and 3 cousins point to a familial tendency to multiple hereditary signs of degeneration.

The relationship of these symptoms to the Laurence-Moon-Biedl syndrome is of special interest. The girl showed three of the five symptoms "required," namely, atrophy of the optic nerve with pigmentary degeneration of the retina, syndactylism and mental retardation, and her condition could therefore be considered an "incomplete" Laurence-Moon-Biedl syndrome.

The five cardinal signs were present in only 24 of the 87 cases reported in the literature as instances of the Laurence-Moon-Biedl syndrome. In the remaining 63 the syndrome must be considered "incomplete." One may object to the inclusion of these cases of the "incomplete" syndrome. However, 3 of the 4 cases of Laurence and Moon (no polydactylism) and 1 of the 2 cases of Biedl (no mental retardation) would then have to be excluded because the syndrome was incomplete. In our opinion the description of cases of the "incomplete" syndrome is not without importance in the etiologic and genetic investigation of such hereditary deviations.

The lack of infundibulopituitary symptoms in the girl seems significant, since it proves that the opinion advanced by some authors that a pituitary or hypothalamic deficiency may be of central importance in the etiology of the Laurence-Moon-Biedl syndrome is not tenable. The retinitis pigmentosa, mental deficiency and syndactylism in this case cannot have been caused by hypothalamic or pituitary changes but were independent hereditary defects.

The occurrence of dwarfism in the 2 brothers can hardly be coincidental. Retarded growth was noted in 3 of the 4 patients described by Laurence and Moon. Shortness of stature was noted in 17 of the 87 cases cited in the literature, while in many descriptions no mention was made of height. Dwarfism in the brothers of Shirley H. apparently could not be attributed to malnutrition, rickets, chondrodystrophy or hypothyroidism or to hepatic, intestinal or renal insufficiency. Their dwarfism was probably due to pituitary dysfunction. If this is true, symptoms of pituitarism, lacking in the sister, were found in the 2 brothers. Such a dissociation of symptoms in a family is often observed in hereditary multiple degeneration.

To discover additional evidence of the questionable unity of the Laurence-Moon-Biedl syndrome, an analysis of the literature usually cited under that name was undertaken. In the table, in addition to the five cardinal signs of the syndrome, "accidental findings," such

as dwarfism, atrophy of the optic nerve without retinitis pigmentosa, strabismus, nystagmus, deafness, congenital heart disease and deformities of the skull, are listed as symptoms of equal importance. Each symptom is designated by a letter, and the frequency of their combination is tabulated. The table is based entirely on cases cited in the literature as instances of the Laurence-Moon-Biedl syndrome. Data on living brothers and sisters of the patients who showed any malformation are included. This procedure was thought to be permissible because the symptoms of these siblings, though they were incomplete from the standpoint of the syndrome, were certainly due to the same cause. We cannot claim completeness for the table, since many authors stated neither the presence nor the absence of certain symptoms which they considered unimportant.

Of the 102 patients whose symptoms were tabulated, only 24 showed the combination of the five required symptoms: obesity, hypogenitalism, retinitis pigmentosa, mental retardation and polydactylism. Therefore, the syndrome of the remainder must be considered "incomplete." On the other hand, in 14 of the 24 cases in which the syndrome was complete, it was "supercomplete"; that is, there were additional heredodegenerative symptoms which could not be considered accidental. Thus ten cases remain in which there were present only the five typical symptoms of the Laurence-Moon-Biedl syndrome.

It is true that in the table the combination ABDIK appears more frequently than any other. However, that does not justify the conclusion that it actually has the highest incidence, since the table is based on cases collected for the purpose of confirming the Laurence-Moon-Biedl syndrome. Probably one would find just as many cases of the other combinations if a search were made for them. This hypothetical statement could have been made more obvious by adding to the table data on a collection of evidently related cases not contained in the literature of the Laurence-Moon-Biedl syndrome. Such a procedure would be justified, since there is a gradual transition from the combinations we have listed to others not thought of in this connection. For example, the association of retinitis pigmentosa and deafness occurs in the table only twice (BDHI and BDHK), the Laurence-Moon-Biedl syndrome being "incomplete" in the cases. Thus an impression might be gained that the combination is rare. This is not the case, as can be seen from Bell's monograph on retinitis pigmentosa, in which she stated that the combination was found in about 10 per cent of 919 cases. On the other hand, the combination of polydactylism and retinitis pigmentosa is found in our table 47 times, or in 66.2 per cent of the cases, while Bell found it in only 1 per cent of her cases of retinitis pigmentosa. These considerations should be carried on for each symptom

The Incidence of Symptoms in Cases of the Laurence-Moon-Biedl Syndrome Reported in the Literature

	Frequency	Author by Whom Reported
ABCD FG	2	Laurence and Moon; Reilly and Lisser
ABCD FG IK M	1	Bertolotti
ABCD G IK	1	Solis-Cohen and Weiss
ABCD I	2	Solis-Cohen and Weiss; Lange
ABCD IK	2	Solis-Cohen and Weiss; Biedl and Raab
ABC E K	1	Rozabel-Farnès
ABC HI	1	Weiss
ABC I	1	Zondek
AB D	3	Looft; Krückman and Meyer; Biedl and Raab
AB D FG K	1	Bernhardt
AB D FG IK	3	Laurence and Moon; McCrae and Weiss; Ricaldoni and Isola
AB D F I	1	Zondek
AB D F IK	1	Beck
AB D G I	2	Rosenstein; Cockayne and others
AB D G IK	6	Lange; Denzler; Ricaldoni and Isola; Sterling
AB D I	3	Ornsteen; Krückman and Meyer; Solis-Cohen and Weiss
AB D IK	10	Gordon; Poos; Looft; Jenkins and Poncher; Orgaz; Bauer; von Jaksch; McAlpine; Beck; Lange
AB D K	5	Herzog; Boenheim; de Schweinitz; Bauer
AB D K M	1	Boenheim
AB E	1	Schweizer
AB EFG K	1	Bernhardt
AB E K	1	Rozabel-Farnès
AB I	1	Weiss
AB IK	1	Molitch and others
AB IK M	1	Turner
A CD G IK	1	McKinney
A CD IK	2	Molitch and others; Looft
A CD K	1	de Schweinitz
A D FG	1	Rowe
A D FG I	1	Reilly and Lisser
A D FG IK	1	Griffiths
A D F IK	1	Lisser
A D F K	1	Bardet
A D G I	1	Cockayne and others
A D G IK	1	Deusch
A D I	4	Menninger; Ornsteen; Reilly and Lisser
A D K M	1	de Schweinitz
A FG I	1	Reilly and Lisser
A F IKL	1	Molitch and others
A G I	1	Cockayne and others
A G IK M	1	de Cyon
A IKLM	1	Grossman
A I	1	Gordon
A K	1	Grossman
BCD FG	1	Laurence and Moon
BCD FG I	1	Laurence and Moon
B D G I	1	Madigan and Moore
B D G IK	1	Cockayne and others
B D HI	1	Boenheim
B D H K	1	Boenheim
D F K	1	Rieger and Trauner
D IK	1	Cockayne and others
D IK M	2	Ssereissky; Pagels
D K	1	Pagels
G I	1	Pagels
H K	1	Weiss
IK	2	Cockayne and others; Lange
K	10	Pagels; de Cyon; Biedl; Biedl and Raab; Rieger and Trauner; Griffiths; Orgaz
KL	1	Deusch

A, obesity; B, genital dystrophy; C, dwarfism; D, retinitis pigmentosa; E, optic atrophy without retinitis pigmentosa; F, strabismus; G, nystagmus; H, deafness; I, mental deficiency; K, polydactylism, syndactylism; L, congenital heart disease; M, deformities of the skull.

and would show what a distorted picture, as far as frequency of combination is concerned, results through the establishment of such a syndrome.

It would be of great value to the clinician as well as to the pathologist, the endocrinologist and the geneticist to know which combinations of hereditary deviations are found together frequently and which are rarely associated. Only an unselected collection of cases, with as complete a family history as possible, and a statistical evaluation on a broad basis will provide that information. The construction of syndromes, which is in most cases an arbitrary procedure, tends to obscure rather than to reveal the true picture.

SUMMARY

1. Cases of an "incomplete" Laurence-Moon-Biedl syndrome have been reported, and the literature has been reviewed.

2. From the evidence thus presented, the designation as a syndrome of the five hereditary symptoms retinitis pigmentosa, obesity, hypogenitalism, mental retardation and polydactylism has been shown to be unjustified.

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REACTION FOLLOWING THE INTRAMUSCULAR INJECTION OF WHOLE BLOOD

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In recent years whole human blood given by intramuscular injection has been used extensively for prophylaxis and treatment. Accidents have occasionally followed such injections. Thus, pyogenic infections have developed at the sites of injection, syphilis and malaria have been transmitted and allergic phenomena, such as urticaria, have been noted. The etiology of such occurrences is usually obvious. In this communication there is reported the study of a group of children in whom a definite reaction appeared after the intramuscular injection of whole blood, the reaction having an almost identical course in all the children in whom it developed. Approximately six days after the injection, the affected children suddenly became acutely ill, with fever and malaise, and the sites of injection became swollen, hot, red and painful. These symptoms lasted for three or four days and then subsided completely. A single reference in the literature to a similar reaction has been found. Kaiser,[1] who injected from 10 to 15 cc. of whole blood intramuscularly into 214 children for prophylaxis of measles, stated briefly:

"Reactions developed in five children. They occurred on the fifth day and were characterized with swelling, local tenderness and fever."

However, from a number of personal communications it would appear that such reactions are not uncommon even though unreported. No reports have been found dealing with the possible etiology of this type of reaction. In this study certain observations have been made which appear to cast some light on the nature of the phenomenon.

The opportunity to observe and study this reaction presented itself in the following manner: From Aug. 20 to Sept. 26, 1932, while Philadelphia was in the midst of an epidemic of acute anterior poliomyelitis, a study was undertaken at the Department for the Prevention of Disease at the Children's Hospital, of the prophylactic use of parents'

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1. Kaiser, D. Albert: Value of Immune Adult Blood in the Treatment of Measles, New York State J. Med. **33**:521, 1933.

whole blood. The results of this investigation have been reported,[2] and they bear no relation to the present study. During this period 1,341 children were given injections of their parents' blood. The technic of injection was as follows:

Two cubic centimeters of a 10 per cent solution of sodium citrate was drawn into a large syringe. By means of the same syringe 60 cc. of the donor's blood was withdrawn, shaken and immediately injected into the child's buttocks, 30 cc. into each side.

Of this group, 52 children showed the reaction already mentioned. A more complete picture of the onset and course of the reaction is given by the following case history of 1 of the 3 children who were admitted to the wards for observation. The remaining children were studied in the outpatient department.

L. S. was a 6½ year old Italian boy. The family history and the past medical history were negative and entirely irrelevant.

The patient and his brother (aged 10) each received 60 cc. of their mother's blood on Sept. 15, 1932, as prophylaxis against poliomyelitis. The brother suffered no ill effects at any time. For some hours following injection, the patient complained of pain in the buttocks which made walking difficult. This disappeared, and the following day he was perfectly well, playing outdoors actively. He continued to carry on his normal activities for the following five days. On the night of September 20, five and one-half days after the injection, he went to bed feeling perfectly well. At 11 p. m. he awakened with such severe pain and tenderness in the buttocks that he could not lie on his back. The mother noted that he was feverish. He slept through the remainder of the night lying on his abdomen. On the morning of September 21 the pain in the buttocks was more intense; the buttocks were red, swollen and very tender, and the fever was evidently higher. He was brought to the hospital and admitted to the ward at that time.

Physical Examination.—The patient was a well developed and fairly well nourished boy, who seemed very ill. He walked with great difficulty with a shuffling gait, as he did not bend his lower extremities at the knees or hips.

The temperature was 102.4 F., the respiratory rate 26 and the pulse rate 120. The skin was warm and dry, with areas of erythema over both buttocks. The mucosa of the nose and pharynx was injected. There was some puffiness of the upper and lower lids of both eyes, and the palpebral and bulbar conjunctivae were injected. In the right eye there was evidence of paralysis of the third nerve which had been present since birth.

Both buttocks were swollen, tender and red—the right buttock more markedly. The swelling had its center around each point of injection, and there was brawny induration of the tissues, with pigskin mottling of the overlying skin. There was tenderness in the back of the thighs, popliteal spaces and calves and along the course of the sciatic nerves.

Laboratory Findings.—The urine was normal on two examinations. The blood on September 21 showed 3,810,000 red cells, 76 per cent hemoglobin and 14,000

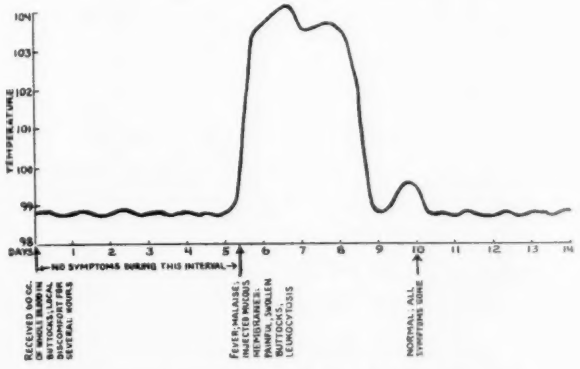
2. Stokes, Joseph, Jr.; Wolman, J. Irving; Carpenter, C. Howard, and Margolis, Julius: Prophylactic Use of Parents' Whole Blood in Anterior Poliomyelitis: Philadelphia Epidemic of 1932, Am. J. Dis. Child. **50**:581 (Sept.) 1935.

white blood cells, with 74 per cent neutrophils, 19 per cent lymphocytes, 1 per cent mononuclears, 3 per cent transitional cells and 3 per cent eosinophils. The Wassermann and Kahn reactions were negative. The spinal fluid was entirely normal. A blood culture gave negative results. The Mantoux reaction was negative to 1 mg. of old tuberculin.

Course.—Warm compresses saturated with magnesium sulfate were applied to the buttocks, and on September 24 the patient was afebrile, the symptoms had disappeared and the buttocks appeared normal.

The blood on September 23 showed 3,640,000 red cells, 72 per cent hemoglobin and 12,250 white cells, of which 70 per cent were neutrophils, 29 per cent lymphocytes and 1 per cent mononuclears. On September 27 there were 6,700 white cells, of which 50 per cent were neutrophils, 46 per cent lymphocytes, 1 per cent mononuclears and 3 per cent eosinophils.

The 2 other children admitted to the hospital suffered from reactions which were replicas of that shown by the first patient.



Temperature curve and clinical findings in case 1.

One, an Italian girl of 5½ years, had received 60 cc. of her father's blood. Two brothers of the patient, 8 and 11 years old, had received similar injections and suffered no ill effects. The patient's reaction occurred 5½ days after injection. The blood showed red blood cells, 4,580,000; hemoglobin, 82 per cent, and white cells, 18,900, with a differential count showing neutrophils, 72 per cent; lymphocytes, 23 per cent, and monocytes, 1 per cent. Other tests gave negative results.

Three days later the leukocytes numbered 9,400, with a differential count of 68 per cent neutrophils and 28 per cent lymphocytes.

The third patient was an Italian girl of 3 years, who had received 60 cc. of her mother's blood. A reaction occurred five days after injection and was similar in all respects to that of the other 2 children. She was not brought to the hospital until the fourth day of the attack, and she recovered in two more days. On the day of admission there were only 9,500 leukocytes, with 70 per cent neutrophils and 28 per cent lymphocytes. Other tests gave negative results.

For all 3 of the patients no family history of allergy could be elicited.

The clinical course of the reaction is shown graphically in chart 1, which presents the temperature curve and clinical findings in case 1.

In table 1 is presented a résumé of the observations on the entire group of children.

From this table the following facts are apparent:

1. Fifty-two of 1,341 children, or 3.87 per cent, showed the reaction. This is in fairly close agreement with the incidence in Kaiser's series, in which 5 of 214 children, or 2.35 per cent, were affected. 2. There seemed to be no significant predilection for either sex. 3. Age seemed

TABLE 1.—*Summary of Clinical Findings in Group of Children with Reaction*

Number of children given injections of whole blood	1,341
Number of children who showed a reaction	52, or 3.87 per cent
Sex distribution of children in whom a reaction developed	
Male	33
Female	19
Time of appearance of reaction following injection	2 to 10 days, average 5.7
Duration of reaction	2 to 7 days, average 3.5
Signs and symptoms of reaction	
Systemic	
Sudden onset	
Temperature 101 to 104 F.	
Malaise	
Injection of mucous membranes	
Leukocytosis	
Local	
Pain and tenderness	
Swelling	
Heat	
Redness	

TABLE 2.—*Age Range of Entire Group and of Children Showing Reactions*

Age, Years	Number of Children Reacting	Percentage of 1,341 Children in Each Age Group
0- 1	0	0.2
1- 2	3	11.5
2- 3	5	12.2
3- 4	5	12.0
4- 5	8	11.1
5- 6	8	12.0
6- 7	4	10.0
7- 8	3	9.1
8- 9	9	8.5
9-10	4	7.1
10-11	3	5.1
11-14	0	1.0

to play no part; the children varied in age from 18 months to 10 years, and their ages were scattered over the age range of the entire group of 1,341 children (table 2).

Several other factors were found to have no bearing on the etiology of the reaction. Thus, color did not seem to be an important factor, since 9 of the 52 children were Negroes and the remainder were white. This corresponded well with the composition of the entire group of 1,341 children, which contained 27 per cent Negro and 73 per cent white children. The sex of the parent who served as donor of the

TABLE 3.—*Results of Typings and Cross-Matchings of Cells and Serums*

Patient	Mother's or Father's Blood Type (Donor)	Patient's Blood Type (Recipient)	Blood Type of Brother or Sister 1	Blood Type of Brother or Sister 2	Cross Matchings of Cells and Serums					
					Donor's Serum + Patient's Cells	Donor's Cells + Patient's Serum	Donor's Serum + no. 1 Brother's/Sister's Cells	Donor's Cells + no. 1 Brother's/Sister's Serum	Donor's Serum + no. 2 Brother's/Sister's Cells	Donor's Cells + no. 2 Brother's/Sister's Serum
7. Bond, E.....♀	3	4	3	3	3 serum + 4 cells No agglutination	3 cells + 4 serum Cells hemolyzed slowly	3 serum + 3 cells No agglutination	3 cells + 3 serum No agglutination	3 serum + 3 cells No agglutination	3 cells + 3 serum No agglutination
9. Bruno, A.....♀	2	3	..	..	2 serum + 3 cells Agglutination	2 cells + 3 serum Agglutination				
12. Crampton, G...♀	3	4	3	..	3 serum + 4 cells No agglutination	3 cells + 4 serum Cells hemolyzed rapidly	3 serum + 3 cells No agglutination	3 cells + 3 serum No agglutination		
15. Delacruz, G.....♀	2	4	2	..	2 serum + 4 cells No agglutination	2 cells + 4 serum Cells hemolyzed immediately	2 serum + 2 cells No agglutination	2 cells + 2 serum No agglutination		
20. Exum, F.....♂	2	4	2	4	2 serum + 4 cells No agglutination	2 cells + 4 serum Cells hemolyzed slowly	2 serum + 2 cells No agglutination	2 cells + 2 serum No agglutination	2 serum + 4 cells No agglutination	2 cells + 4 serum Agglutination
23. Guzzi, R.....♀	3	4	3	3	3 serum + 4 cells No agglutination	3 cells + 4 serum Cells hemolyzed immediately	3 serum + 3 cells No agglutination	3 cells + 3 serum No agglutination	3 serum + 3 cells No agglutination	3 cells + 3 serum No agglutination
24. Harris, R.....♂	2	4	4	..	2 serum + 4 cells No agglutination	2 cells + 4 serum Agglutination	2 serum + 4 cells No agglutination	2 cells + 4 serum Agglutination		
25. Hill, D.....♀	3	2	..	..	3 serum + 2 cells Agglutination	3 cells + 2 serum Agglutination				
32. Pendleton.....♂	3	4	2	..	3 serum + 4 cells No agglutination	3 cells + 4 serum Cells hemolyzed slowly	3 serum + 2 cells Agglutination	3 cells + 2 serum Agglutination		
33. Principato.....♀	3	4	..	..	3 serum + 4 cells No agglutination	3 cells + 4 serum Cells hemolyzed slowly	Sisters ↕ Sisters			
34. Principato.....♀	3	4	..	..	3 serum + 4 cells No agglutination	3 cells + 4 serum Cells hemolyzed slowly				
36. Sample.....♂	2	4	2	2	2 serum + 4 cells No agglutination	2 cells + 4 serum Cells hemolyzed immediately	2 serum + 2 cells No agglutination	2 cells + 2 serum No agglutination	2 serum + 2 cells No agglutination	2 cells + 2 serum No agglutination
37. Sangiorgio.....♂	2	4	2	..	2 serum + 4 cells No agglutination	2 cells + 4 serum Cells hemolyzed immediately	2 serum + 2 cells No agglutination	2 cells + 2 serum No agglutination		
40. Stokes, D.....♂	2	4	..	..	2 serum + 4 cells No agglutination	2 cells + 4 serum Cells hemolyzed immediately				
42. Tavani.....♀	2	4	2	4	2 serum + 4 cells No agglutination	2 cells + 4 serum Cells hemolyzed immediately	2 serum + 2 cells No agglutination	2 cells + 2 serum No agglutination	2 serum + 4 cells No agglutination	2 cells + 4 serum Agglutination
47. Weiss.....♀	2	3	1	..	2 serum + 3 cells Agglutination	2 cells + 3 serum Cells hemolyzed slowly	2 serum + 1 cell Agglutination	2 cells + 1 serum No agglutination		
49. Zeller.....♂	2	4	..	..	2 serum + 4 cells No agglutination	2 cells + 4 serum Agglutination				

blood was of no import, there being 25 fathers and 27 mothers; nor did the sex of the parent in relation to the sex of the child seem of any significance.

EXPERIMENTAL STUDIES

In an attempt to elucidate the nature of this reaction the following studies were carried out: 1. Intradermal tests were performed on the reacting child with various fractions of the donor's blood. 2. Typings and cross-agglutinations of reacting and nonreacting children with their donors were studied. 3. A reproduction of the reaction in a reacting child was studied.

Intradermal Tests.—One-tenth cubic centimeter of each of the following was injected intradermally into the skin of the forearms:

1. Whole blood
2. Citrated whole blood
3. Washed corpuscles *
4. Serum
5. Citrated serum (3 per cent)
6. 3 per cent sodium citrate

} from donor

* Resuspended in physiologic solution of sodium chloride.

These studies were carried out on 5 children and their nonreacting brothers and sisters, and in all instances the results were negative.

Typings and Cross Agglutinations: For 17 of the group of 52 children, the type of blood of the child as well as that of any brother or sister who received an injection from the same donor and did not react and of the blood of the donor was determined. Microscopic cross-agglutination tests were performed, using cells and serum of child and donor. One drop of serum plus 1 drop of a 5 per cent suspension of the corpuscles was used. The results are summarized in table 3. The Moss nomenclature for blood types is used.

From the table the following facts are apparent:

1. The donor's red corpuscles were incompatible with the reacting child's serum in all 17 cases. The distribution of incompatibilities is shown in table 4.

2. In 13 of the 17 children, the donor's corpuscles were hemolyzed by the child's serum before agglutination could occur.

3. Incompatibility of the donor's cells and the recipient's serum did not invariably lead to a reaction: Thus, 4 of the reacting children had a brother or sister who was given an injection of the same donor's blood and who did not react. The serum of the brother or sister was incompatible with the cells of the donor in these 4 cases (table 5).

Reproduction of the Reaction: L. S., whose history is given in case 1, was readmitted to the hospital on Aug. 4, 1933, approximately eleven months after his reaction. Cutaneous tests were performed again with the fractions from the mother's blood, mentioned before, and all gave negative results.

Typing of the blood showed that his was of type 4, while that of his mother was of type 2.

Cross-agglutination tests showed that the patient's serum agglutinated his mother's corpuscles, but there was no hemolysis of the cells. His cells were not agglutinated by his mother's serum—findings in keeping with the blood types of the patient and his mother.

On August 15 he was given an injection of 35 cc. of citrated serum obtained from his mother. No reaction followed this injection, and the cutaneous tests and cross-agglutination tests gave the same results as before injection.

On August 25 he was given an injection of 60 cc. of citrated whole blood from his mother. Twenty-eight hours after this injection the temperature rose suddenly to 102.8 F., and both buttocks became swollen, red, hot and painful. The temperature continued elevated to 102 F. for four days, and the buttocks remained swollen for three days, after which they both became normal.

Cutaneous tests with the fractions of the blood again gave negative results. Cross-agglutination tests performed on August 31 and September 1 showed no hemolysis, only agglutination of the donor's cells by the patient's serum. Unfor-

TABLE 4.—*Distribution of Incompatibilities Between Cells of Donor and Serum of Reacting Child*

Type of Donor's Blood	Type of Child's Blood	Number of Cases
2	4	8
3	4	6
2	3	2
3	2	1

TABLE 5.—*Incompatibilities Between Cells of Donor's Blood and Serum of Sibling of Reacting Child*

Type of Donor's Blood	Incompatible Type of Blood of Child Who Reacted	Incompatible Type of Blood of Brother or Sister Who Did Not React	Family
2	4	4	Exum
2	4	4	Harris
3	2	4	Pendleton
2	4	4	Tavani

tunately, the patient was discharged from the hospital through a mistake before further tests for hemolysis could be performed, and later tests were not possible. It seems probable from the other data that hemolysin would have appeared later. The reaction which developed after the intramuscular injection of whole blood on this occasion was similar to the first reaction, eleven months before. However, this second reaction developed more quickly than the first, since it occurred twenty-eight hours after injection, while the first began five and one-half days after injection. After the first reaction there was demonstrable hemolysin against the donor's corpuscles, while no hemolysin was present after the second reaction during his stay in the hospital. As mentioned, hemolysin may readily have been present at a later date.

Whatever might have been the nature of the substance calling forth the reaction, it did not appear to be in the serum of the donor, for

no reaction developed after the injection of the serum. Since the symptoms developed after the injection of whole blood, it may be inferred that the substance resided in the donor's red cells.

COMMENT

Of the 17 children whose blood was investigated, all showed this finding in common: Their serum agglutinated the cells of the donor. This might possibly be a coincidence, but it seems highly unlikely. However, it cannot be concluded from this finding that incompatibility of a recipient's serum with a donor's cells will always lead to a reaction following the intramuscular injection of blood. Surely more than 52 such incompatibilities would have occurred in a group of 1,341 injections, and what is more conclusive, the blood of some of the brothers and sisters of reacting children was similarly incompatible with that of their donors and they did not show reactions.

In connection with this point of incompatibility, the case of one child, D. S., is of extreme interest. Six months prior to the development of his reaction, he had received 30 cc. of blood from his father intramuscularly as prophylaxis for measles (the blood of both the father and the patient was of type 4) without any ill effect. However, when he received blood from his mother (type 2) a typical reaction developed. This appears to be strong evidence that the reaction is related to the incompatibility of the recipient's serum and the donor's cells.

The donor's serum can be eliminated as a possible etiologic agent in this reaction. Thus, in the case of L. S. injection of his mother's serum was harmless. Furthermore, hundreds of injections of human serums have been given at the Children's Hospital without the development of reactions of this type; nor has there been any description in the literature of such reactions following the injection of human serum, free from hemoglobin.

As noted, 13 of the 17 children showed hemolysin in their serum against the corpuscles of their donors. While no titrations of this hemolysin were attempted, it appeared to be present in fairly high titer, because in all instances the hemolysis took place before agglutination could occur. Isohemolysins occur normally in healthy persons. Thus, Jones [3] has shown that 27.3 per cent of new-born infants have isohemolysins in their serum, and Hesser [4] demonstrated that 44 per cent of adults possessed them.

3. Jones, Basil B.: Isohemolysins in Human Blood, with Especial Reference to the Blood of the New-Born, Am. J. Dis. Child. **22**:598 (Dec.) 1921.

4. Hesser, S.: Serologic Studies of Human Red Corpuscles, Acta med. Scandinav. (supp.) **9**:1, 1924.

The hemolysins present in the serums of these 13 children were probably an increase of normally occurring isohemolysins, in response to the injection of incompatible blood corpuscles. Thomsen [5] injected incompatible blood intramuscularly into 56 persons. He found no increase in the titer of agglutinins against the injected corpuscles. He mentioned a reaction in 1 case, with fever and local swelling and pain, which disappeared in three or four days, without stating how long after the injection this occurred. In 8 persons he found a marked increase in the hemolytic titer of the blood. The hemolysin which was demonstrable in his cases hemolyzed not only the corpuscles of the blood with which the injections were made (type 2) but also the corpuscles of blood of type 3. Evidently the injection of incompatible corpuscles not only stimulates the formation of hemolysin against the type of corpuscle injected but causes an increased formation of other naturally occurring hemolysins. Unfortunately, the serums of our patients were not tested against the corpuscles of types different from that of the donor.

Thomsen also followed the titer of a similar hemolysin which developed in one patient after a mismatched blood transfusion. This hemolysin was present in high titer eleven and nineteen days after transfusion, but when the third test was made, three months later, it was absent. This observation may explain the absence of hemolysin in 4 of the 17 children of the present study. They may have been tested too long after their reaction, the tests having been done four and one-half weeks, six and one-half weeks, eight weeks and nine months, respectively, after the reactions in these 4 cases, while in the 13 cases in which hemolysin was noted, the tests were done within four weeks after the reaction. Thus, it is possible that the hemolysin had disappeared in the 4 cases in which it was not demonstrated.

The fact that L. S., in whom the reaction was reproduced, did not show hemolysin after his second reaction is not readily explained. It is possible that he was tested too early, one day and two days, respectively, after the reaction. During the reaction and shortly thereafter it is highly likely that the hemolytic antibodies were fixed at the sites of injection by residual antigenic substance, that is, the foreign blood cells, or by altered tissue cells, so that they were not demonstrable in the general circulation. As mentioned, he was discharged from the hospital by mistake.

SUMMARY

Of a group of 1,341 children given injections of citrated whole blood intramuscularly, 52 showed fever, malaise and leukocytosis, with

5. Thomsen, O.: Immunisierung von Menschen mit arteigenem, gruppenfremden Blute, Ztschr. f. Rassenphysiol. **2**:105, 1930.

swelling, redness and pain at the sites of injection for from two to ten days, average five and seven-tenths days, after the injection. These symptoms lasted from two to seven days (average three and one-half days) and left no residua.

This reaction was independent of sex, age or color.

The blood types of 17 of the children and the blood types of the donors were investigated. In every case the types were such that the cells of the donor were incompatible with the serum of the recipient.

The blood of 13 of these 17 children possessed hemolysin against the donor's corpuscles.

The possible significance of these findings is discussed.

A CLINICOPATHOLOGIC STUDY OF SEXUAL PRECOCITY WITH HYDROCEPHALUS

REPORT OF TWO CASES OCCURRING IN FEMALES, WITH POSTMORTEM OBSERVATIONS IN ONE

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Sexual precocity, always of interest to the clinician, has become increasingly so of late, because of a more thorough appreciation of the causative factors. Notwithstanding the progress made in this field, there are still cases of precocity associated with lesions of the brain which require further elucidation. Particularly is this true of that type of precocity associated with lesions in the hypothalamic region or with lesions of the brain which are accompanied by chronic increased intracranial pressure and which produce their effects through some disturbance in the hypothalamic-hypophysial mechanism, without producing the ensuing typical lesions in the endocrine glands one generally associates with sexual precocity.

Although some clinicians may doubt that there is any connection between such lesions of the brain or intracranial pressure and their effects on the hypothalamic-infundibular-hypophysial pathway and precocity, others have hinted at the possibilities of such lesions in association with involvement of the pituitary gland. Heuyer, Le Marquand and others have considered the likelihood of such derangement of the pituitary gland in the following cases:

Heuyer and his co-workers,[1] in 1931, presented the case of a boy with moderate hydrocephalus, who showed signs of physical and sexual precociousness. At postmortem examination, no gross lesions of the adrenal glands or of the testicles were found. Macroscopically, the pineal body and the hypophysis were found to be normal. In the region of the mamillary tubercles a well defined tumor was present which

From the Endocrine Clinic of the Department of Pediatrics, New York University College of Medicine, and the Children's Medical Service of Bellevue Hospital, Dr. Charles Hendee Smith, Director.

1. Heuyer, G.; Lhermitte, J.; de Martel and Vogt, C.: A Case of Precocious Macrogenitosomia Associated with an Ependymal-Glioma in the Mamillo-Tuberal Region, Rev. neurol. **2**:194, 1931.

pressed on and flattened the pituitary gland anteriorly. Serial histologic sections of the entire cerebral trunk revealed an ependymoglioma, developed at the expense of the mamillary tubercles, especially the right. This infiltrated the infundibulotuberal region, but did not produce any appreciable destruction of the nuclei of this region. These authors admitted that it was permissible to suppose that a tumorous change which caused no degeneration and no necrosis may have acted by possible excitation of the nervous system, which was reechoed in the hypophysis.

Recently, Le Marquand [2] presented the case of a boy aged 4½ years, who showed true precocious puberty but did not have hydrocephalus. He was studied from the age of 14 months. Necropsy revealed a circumscribed tumor occupying the interpeduncular space and attached to the right corpus mamillare and the tuber cinereum. The tumor appeared to occupy a redundant portion of the floor of the ventricle and appeared to be formed by a developmental error (this Le Marquand called a hamartoma). On microscopic examination the adrenal glands, the pineal body, the thymus, the pancreas, the thyroid gland and the parathyroid glands appeared to be normal. The testes contained conspicuous groups of interstitial cells; spermatids and spermatozoa appeared in the lumens of the tubules. Serial sections of the hypothalamus and the pituitary body revealed no abnormalities. This author felt that the only pathologic change to which the precocious puberty could be ascribed in this case was the tumor-like mass at the base of the brain. He also suggested that in cases in which the pineal body, the adrenal glands, the hypothalamus or the gonads were involved, each or all caused pubertas praecox by an influence on the hypothalamic centers, the latter effects then influencing the pituitary body.

Krabbe [3] described the case of a boy who showed pubertas praecox. In addition, he showed tuberous sclerosis of the brain which manifested itself by the formation of gliomas in the mamillary bodies and in the ventricles by internal hydrocephalus. Postmortem examination, gross and histologic, revealed that the thymus, thyroid, pituitary and adrenal glands showed no abnormalities, yet the testicles showed spermatozoa. The amount of connective tissue in the testes corresponded to the normal amount in an adult; the interstitial cells were a little more numerous than in an adult.

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2. (*a*) Le Marquand, H. S.: Suprarenal Virilism, Proc. Roy. Soc. Med. **25**:804, 1932. (*b*) Le Marquand, H. S., and Russell, D. S.: A Case of Pubertas Praecox, Roy. Berkshire Hosp. Rep., March 1934-1935, p. 31.

3. Krabbe, K. H.: Tuberous Sclerosis of the Brain and Hydrocephalus in Their Relationship to Precocious Puberty, Encéphale **17**:281, 1922.

Several other cases of macrogenitosomia or precocious puberty associated with a tumor of the floor of the third ventricle or of the hypothalamic region and hydrocephalus in boys have been described by Horrax and Bailey,[4] Schmalz,[5] Dods,[6] Thomas Schaeffer[7] and others.

Schlesinger[8] reported the case of a girl 8 years and 8 months of age whose breasts began to develop at the age of 7. The secondary sexual characteristics were present, but menstruation had not begun. She presented progressive hydrocephalus due to postbasilar meningitis at the age of 4 months and subsequent spastic paralysis. The diagnosis was not verified pathologically.

De Cardenas[9] reported the case of an 8 year old girl with spastic paralysis who as a result of meningitis at an early age showed progressive enlargement of the head since the age of 2. When she was 3 years of age her breasts began to enlarge, and pubic hair made its appearance. The labia were enlarged, and the clitoris was well developed. (It was not stated whether the clitoris was penis-like or whether menstruation was present.) However, after injection of the patient's urine into immature female mice, a study of the animals revealed no enlargement of the ovaries, no corpora lutea and no hemorrhagic cysts but did reveal increased development of the follicles as well as great congestion of the tubes and ovaries, which we believe were probably effects of the follicle-stimulating hormone. Injection of the patient's urine into male rats caused no apparent external changes, but autopsy revealed a diminution in the size of the seminal vesicles and testicles, which we believe were probably the effects of estrogen.[10] De Cardenas expressed the opinion that there must have been some derangement in the function of the hypophysis and the pineal gland as a result of the meningitis with its subsequent hydrocephalus.

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4. Horrax, G., and Bailey, P.: Tumors of Pineal Body, Arch. Neurol. & Psychiat. **13**:423 (April) 1925.

5. Schmalz: Beitr. z. path. Anat. u. z. allg. Path. **73**:168, 1924.

6. Dods, L.: Adenohypophyseal Dystrophies of Infants and Childhood, M. J. Australia **2**:277 (Sept. 1) 1934.

7. Thomas, A., and Schaeffer, H.: Precocious Macrogenitosomia with Hydrocephalus, Inflammatory Lesions of Tubero-Infundibular Lesion and Cervical Trimeningeal Symphysis, Rev. neurol. **2**:595, 1931.

8. Schlesinger, B.: Hydrocephalus with Precocious Puberty Following Post-Basic Meningitis, Proc. Roy. Soc. Med. **28**:149, 1934.

9. de Cardenas, J.: Hydrocephalus and Genital Precocity, Pediatría espań. **21**:600, 1932.

10. Allen, E.: The Ovarian Follicular Hormone, in Sex and Internal Secretions, Baltimore, Williams & Wilkins Company, 1932, p. 393.

Moniz and Lima,[11] in 1932, reported the case of a 9 year old girl in whom hydrocephalus developed shortly after an attack of "meningitis" at the age of 3 months. She had "always been paraplegic." At the time of examination macrogenitosomia was present, and thick cranial bones were noted on roentgen examination. When the child was 9½ years of age, while she was at the hospital, the first menstrual period started. No evident cause for the pubertas praecox could be found, and although necropsy was not performed, the authors felt that the thick cranial bones in hydrocephalus played a possible part in aggravating the intracranial pressure. However, they could not correlate the thickness of the skull with the macrogenitosomia. Interestingly, the photograph of the child in the authors' report bears a striking likeness and is somewhat similar in type to our patient A. D. (case 2).

In addition, the condition in the cases to be cited by us resembles clinically, in so many respects, that in the three cases presented by Schlesinger, de Cardenas, and Moniz and Lima that it is hoped that this report, in which the diagnosis in one case was confirmed by necropsy, and the conclusions may be a step in the direction of further diagnostic clarification.

REPORT OF CASES

CASE 1.—L. M., a 7 year old white girl of Italian parentage, was admitted to the orthopedic service of the Brooklyn Jewish Hospital for the correction of talipes equinus and kyphosis. In addition to these deformities, she presented marked hydrocephalus and precocious development.

The patient was delivered by forceps and weighed 8 pounds (3,628 Gm.) at birth. The father and mother were in good health. The patient was the second born, the first child having died of erythroblastosis foetalis one day after birth. The patient's first tooth appeared at the age of 7 months, and she spoke at an early age. There were no childhood diseases or history of meningitis. Cod liver oil was given during her infancy. The patient had not been able to sit up alone because of a weak back, and when she was supported in a sitting position the weight of her enlarged head apparently caused her to become dizzy. She never had walked because of the talipes equinus and the spasticity of the lower extremities. The mother stated that since birth the child's right foot had "turned in." This condition progressively had become more pronounced as the child grew up, and now this was true also of the left foot. At one time the child could stand up momentarily by supporting herself, but later she could not do even this. Tenotomy had been performed with fairly good results.

The enlargement of the head had been noted at the age of 2 months and had become progressively worse. There was no antecedent acute illness or violent trauma except at the time of the instrumental delivery.

The child had been followed in the outpatient department since the age of 2 years, and her condition had become worse. The enlargement of the head had

11. Moniz, E., and Lima, A.: Paraplegia and Precocious Macrogenitosomia in Congenital Hydrocephalus Accompanied by Thick Cranial Bones, Rev. neurol. **1**:693, 1932.

become so great that the patient had difficulty in supporting it. The hydrocephalus interfered with the upward gaze and seemed to be pushing the eyes downward.

The appearance of suprapubic hair was noted by the mother when the child was 6 years old. Also, since infancy some blond down had been noticed on the child's legs, thighs, forearms and back; there was none on the face, chest or abdomen. In the past year, the breasts had become definitely fuller. Menstrual vaginal bleeding had not appeared, but the mother had noticed a whitish yellow discharge on the child's bloomers.

Physical examination of the child at the age of 7 years showed a fairly alert and well nourished, not acutely ill girl. The body length was 125 cm. The head was markedly enlarged, measuring 72 cm. in circumference. The fontanels were

Fig. 1 (case 1).—Photograph of L. M., at 6½ years of age, showing the marked enlargement of the head, the suggested fulness of the breasts and the bilateral equinus deformities. Pubic hairs are not visible in the photograph as they were shaved in preparation for operation.

closed. An abundant crop of hair was present on the head. There was no hypertrichosis of the face. The eyes were equal and reacted to light. No palsy of the ocular muscles was present; the vision was poor, but there was no nystagmus. The upward gaze was limited by the hydrocephalus. Examination of the fundi showed primary atrophy of the optic nerves. The nose and throat were normal. The teeth showed an eruption commensurate with the child's age, but several teeth presented hypoplasia of the enamel. Hearing was not impaired, and the child's responses were prompt and intelligent; at times she even anticipated the examiner's question.

The heart and lungs were normal. The blood pressure was 110 systolic and 80 diastolic; the pulse ranged from 118 to 130. There was definite kyphosis. The breasts were definitely fuller than normal for the child's age. The nipples were not prominent, and the areolae were pigmented for about 1 inch (2.5 cm.) in diameter. There was no hypertrichosis in the mammary region or on the chest. The axillary region showed slight pigmentation, but no hair.

The abdomen was soft and adipose, but presented no palpable masses. There was a good crop of long black suprapubic hairs of feminine distribution. The external genitals appeared to be mature, and long black hairs were present on the labia majora; the clitoris, although prominent, was not penis-like in type. Rectal examination revealed no mass in the adnexa uteri.

The lower extremities showed spastic paralysis and talipes equinus. There was some hyposensitivity to light touch all over the lower extremities, but the patient's reaction was more acute to firmer pressure. Temperature perception was good. There were some blond hairs on the lower extremities and the forearms. There was some slight weakness of the upper extremities.

The tendinous reflexes were hyperactive, and ankle clonus was present bilaterally. There was no weakness of the muscles of the bladder or rectum; adiadokokinesis or astereognosis was not present. The cranial nerves were intact. The mentality, although fair, was somewhat retarded for the average child of the same age. The impression of the neurologist was that this picture was due to a chronic inflammatory adhesive process at the base of the brain with internal hydrocephalus as the result of trauma at birth.

The laboratory data were as follows: The Wassermann and Kahn tests of the blood were negative. There were 3,500,000 red blood cells, 6,300 white blood cells, with a normal differential count, and a hemoglobin content of 74 per cent. The vaginal smear was negative for Gonococcus. The Mantoux test was negative. The blood during fasting showed chlorides, 338 mg. per hundred cubic centimeters; nonprotein nitrogen, 28 mg.; cholesterol, 182 mg.; sugar, 82 mg.; serum calcium, 10.6 mg.; serum phosphorus, 3.1 mg.; total serum protein, 7.05 per cent; serum albumin, 4.15 per cent, and serum globulin, 2.90 per cent. The albumin-globulin ratio was 1.43.

The urine from the patient was injected into immature female mice, but the ovaries of these animals showed no macroscopic changes.

Roentgenograms of the skull showed tremendous cranial distention in all directions. The fontanels were closed. The cranial tables were intact but thickened. There was loss of vascular markings. The sella turcica was deepened and slightly enlarged. The posterior clinoid processes were thickened and erect. The anterior clinoid processes could not be defined. There were no erosions. The osseous age was moderately advanced for a 7 year old child. There was marked diffuse osteoporosis in the bones of the feet, which was considered to be due to disuse.

When last seen the patient had had an operation for talipes equinus and was progressing satisfactorily.

CASE 2.—A. D. aged 6½ years, American born, was the first and only offspring of healthy Italian parents. The mother began to menstruate at the age of 13 years and was in no way sexually precocious. The patient had been a full term infant, delivered spontaneously, the labor lasting fourteen hours. The condition of the child at birth was good; there was neither cyanosis nor convulsions. She was breast fed for ten months. Her additional diet was prescribed in the outpatient department of the university, to which she was brought on Oct. 12, 1928, at the age of 6 months, because the size of her head had been increasing.

At the age of 2 months the patient was said to have had meningitis. This diagnosis was made by the family physician and a pediatrician. She was acutely ill, having a high fever and convulsions for one week. A grave prognosis was given. After two months of this illness the patient recovered from her acute condition, but in the latter part of this period her head began to enlarge, and it continued to do so until the age of 2 years. Previous to this time the child had been thin, but soon she became plump and appeared to be well nourished. The mother stated that as a result of the foregoing illness, the child was blind for three months, could not move her lower extremities and was somewhat rigid. The rigidity, however, seemed to improve gradually, and in time the child could take a few steps when sufficiently supported.

She had measles at 4½ years and scarlet fever at 5. At the age of 5 years her breasts had enlarged, but the mother thought this to be part of her general

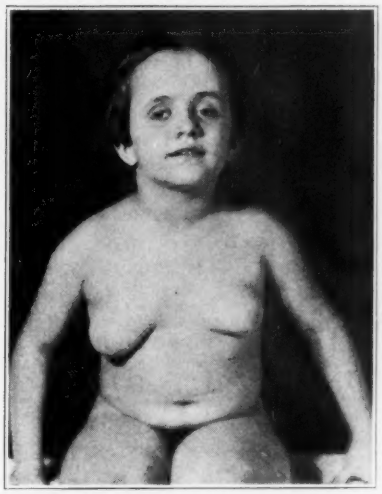

Fig. 2 (case 2).—Photograph of A. D. at 6½ years of age, showing the enlargement of the head, well developed breasts and pubic hair.

plumpness. This change, plus the presence of axillary and pubic hair, was first noticed in the clinic on May 11, 1933. Subsequently the child's voice took on a more mature pitch. The head had not increased further in size after the age of 2.

It was noted by the mother that when the child was 5½ years of age her left foot had turned inward, and for the preceding few months her feet and legs had been getting more spastic. Examination at this time at the orthopedic clinic showed spastic paraplegia and talipes equinus of both feet in addition to hydrocephalus and precocious sexual development. Tenotomy was performed for the deformity of the left foot, and for a time the deformity appeared corrected, only to recur after several months. The child was readmitted to the hospital ten months later for further correction. The upper extremities at this time showed slight flaccidity. A positive Babinski sign was present bilaterally.

During the child's stay in the orthopedic service, purulent otitis media developed on the left side, which was still present when she was transferred to the

pediatric service for further study. At this time examination revealed a mentally retarded but physically well developed, obese child 6½ years of age, who did not appear to be acutely ill. Her height was 48 inches (121.9 cm.) and her weight 75 pounds (34.019 Gm).

Hydrocephalus was marked, the head measuring 64.8 cm. in circumference. There was frontal and parietal bossing; the fontanels were apparently closed.

The pupils were equal and regular and reacted to light, but due to the patient's mental retardation, cooperation for accommodation was lacking. There was a defect in the upward gaze, but no palsy of the external ocular muscles. The vision was fair, although definitely impaired. Some coarse horizontal nystagmus was present, which was more marked on looking to the right or the left. There was no increase in the ocular tension. Fundoscopic examination showed partial atrophy of the optic nerves. The retinal vessels appeared to be normal.

There seemed to be unimpairment of hearing to voices and loud noises. The child's retarded mental state, however, prevented cooperation for more delicate tests. There was a malformation of both bony canals to the extent that the ear drum was visualized as through a small slit. A profuse purulent discharge filled the left external auditory canal.

The dental status corresponded to the chronological age of the child. The tongue was thick and deviated to the left when protruded.

The tonsils were enlarged, as were also some of the anterior cervical glands. The nasal cavities were clear.

There was no rigidity of the neck, nor were any masses felt in this region.

The mammary glands were fairly well developed and showed the presence of some glandular tissue. The areolae were not pigmented, and the nipples were inverted. Some axillary hair was present. The lungs were clear. The heart was apparently normal. The pulse was regular, and the rate was normal. The blood pressure was 102 systolic and 70 diastolic.

Abdominal palpation revealed no masses. The skin was clear and of normal texture; no striae were present. A good crop of long black suprapubic hair of feminine distribution was present. The external genitals appeared to be mature. The clitoris was pubertal in type but in no way penis-like. There were no apparent abnormalities of the pudendal region. Rectal examination revealed the cervix in a posterior position. The fundus uteri was anterior in position and of normal size. The adnexa uteri were normal.

Except for the presence of some axillary hair and a luxurious growth of suprapubic hair, there was no unusual pathologic hirsuties. There was, however, a moderate down on the upper and lower extremities. There was an abundant crop of hair on the head, but none on the face or chest.

The patient's mentality was markedly retarded. Although 6½ years of age, she knew only her name, a few letters of the alphabet and the numbers from 1 to 5. She knew she was in a hospital but could not distinguish between the nurse and the doctor. She could not obey simple commands. She spoke with a rather deep voice.

The child was rather hyposensitive to pain. Her tendinous reflexes were hyperactive bilaterally. The Babinski sign and ankle clonus were positive bilaterally. The abdominal reflexes were all absent. The condition of her lower extremities was described in the history; in addition, there was an operative scar over the left achilles tendon. The upper extremities were flaccid. The impression of the examining neurologist was that disease of the upper motor neuron was present bilaterally.

The laboratory data were as follows: The temperature and pulse and respiratory rates were in general normal. The blood pressure ranged from 108 systolic and 86 diastolic to 100 systolic and 72 diastolic. The Mantoux test was negative with 0.2 mg. of tuberculin. The urine was normal chemically and microscopically. The white blood cells numbered 14,000, with 80 per cent polymorphonuclears and 20 per cent lymphocytes. The red blood cells numbered 4,880,000, with 13.4 Gm. of hemoglobin. The vaginal smear was negative for gonococcus. The Wassermann test of the blood was negative. The Wassermann test and the colloidal gold test of the spinal fluid were negative. Examination of the blood after fasting revealed the following composition: cholesterol, 180 mg. per hundred cubic centimeters; chlorides, 464 mg.; sugar, 99.8 mg.; serum calcium, 9.7 mg., and serum phosphorus, 6.3 mg.

A sugar tolerance test gave the following results: a specimen of blood taken after fasting showed 102 mg. of blood sugar per hundred cubic centimeters of blood. one-half hour after the administration of dextrose the blood sugar content was 142.1 mg. per hundred cubic centimeters; one and a half hours after, 128.1 mg.; two and a half hours after, 96.5 mg., and three and a half hours after, 96.8 mg. Samples of urine taken at the same time as the specimens of blood were found to contain no dextrose or albumin.

Roentgenograms showed the following picture: The skull was markedly increased in size, the maximum anteroposterior diameter being 24.2 cm. The bones of the vault were thinner than normal. There were definite convolutional impressions in the inner table of the posterior parietal and occipital bones. There were no intracranial calcifications or diastases of the sutures. Both mastoids were of the mixed cell, pneumatic type and presented periantral sclerosis. The sella turcica was somewhat flattened and slightly elongated anteroposteriorly; there were no apparent erosions of the clinoid processes or of the floor of the sella.

Ventriculograms were taken after 1,100 cc. of cerebrospinal fluid had been withdrawn and 1,000 cc. of air injected. These showed the ventricles to be distended enormously and to be occupying nearly the entire cranial vault. In the lateral view a band of tissue was seen apparently bisecting the lateral ventricles and separating the anterior horns to a greater extent than normally. The meningeal and other structures in the midfossa were unusually dense.

Roentgenograms of the centers of ossification and the epiphysial nuclei showed an advanced osseous age, equivalent to that of a 13 year old child instead of one 6½ years old. Roentgenograms of the dorsal, lumbar and sacral portions of the spine and pelvis were normal.

Subsequent to ventriculography, the child gradually became stuporous, and signs of aspiration pneumonia developed, which caused her death on the fifteenth day.

Necropsy performed by Dr. Eugene Clark eighteen hours later revealed the following pertinent data: The external aspect of the body conformed to the description given in the clinical examination. The body was 4 feet in height and weighed 75 pounds. The child appeared older than 6½ years of age.

The head was markedly enlarged, measuring 64 cm. at the fronto-occipital circumference, 62 cm. at the suboccipitobregmatic circumference and 68.5 cm. at the submento-occipital circumference. The greatest anteroposterior and transverse diameters of the head were 21 and 16 cm., respectively.

The hair on the head was black and abundant. There was no evident hypertrichosis. The axillary and pubic hair were present in normal female distribution. The body was well developed and well nourished. There were no other significant external findings.

There was an incision about 1 cm. in length in the posterior superior parietal region of the scalp, and a circular trephine opening 1 cm. in diameter was seen on the superior posterior right parietal region. When the calvarium was removed it was found to be 3 mm. in thickness anteriorly and 4 mm. posteriorly. The dura of the calvarium appeared smooth and glistening and was not thickened, and there was no apparent fluid in the subarachnoid space. The dorsal areas of the brain were smooth and flattened; there was no apparent thickening of the leptomeninges. The cerebral cortex was distended, flattened and fluctuant, and the corpus callosum thin. No masses were found in the region of the midbrain. Corresponding to the trephine opening in the skull, there was a wound in the cortex, which appeared to be closed.

After removal of the brain, no fluid was found in the subarachnoid space of the posterior fossa, but stringy adhesions were seen between the pia and arachnoid

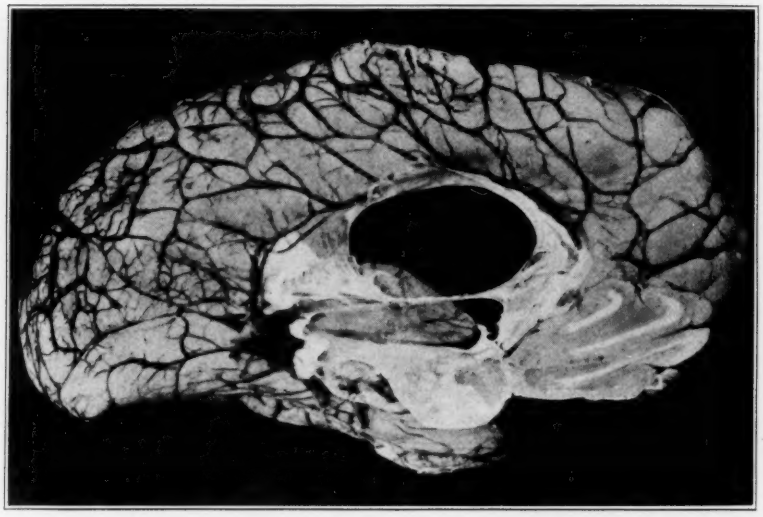

Fig. 3 (case 2).—Midsagittal section of the brain. Note the marked dilatation of the third ventricle. The septum pellucidum has been torn and folded up to show marked dilatation of the lateral ventricles.

and the dura around the basal portion of the cerebellum. The leptomeninges at the base of the brain posteriorly in the region of the cisterna pontis and the cisterna interpeduncularis showed marked thickening. When the brain was removed, the cerebellum and medulla were separated from the bone and the midbrain in the region of the peduncles. About 120 cc. of clear fluid gushed from the ventricles when they were punctured on removal.

After fixation, the brain exhibited well marked hydrocephalus. There was great distention of the frontal lobes and to a lesser degree of the temporal lobes, with hydrops of the third ventricle. The pia-arachnoid over the pons and the surface of the cerebellum and the medulla appeared much thickened. On sagittal section a small remnant of the pineal gland was found. Marked pressure atrophy of both mamillary bodies was noted; they were reduced to thin shell-like

structures. Marked distention of the lateral ventricles and the fourth ventricle was also noted, and the ependyma presented a granular appearance. The corpus callosum was represented by a thin sheet of tissue.

After the abdomen was opened, the fat layer was 2 cm. in thickness and the musculature was well preserved and red-brown. The peritoneum was normal and contained no free fluid.

The pleural sacs were normal. The thymus did not appear to be enlarged and weighed 7.5 Gm. Except for numerous rather well circumscribed firm areas, resembling fresh pneumonic consolidations in all the lobes, the lungs showed no changes.

The heart was not enlarged and weighed 90 Gm. The pericardium was normal; the chambers, valves and musculatures showed no changes that were visible to the naked eye.

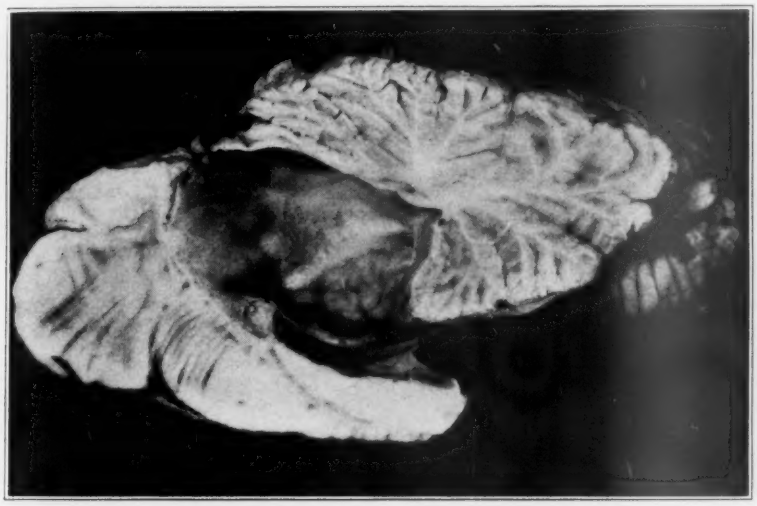

Fig. 4 (case 2).—Midsagittal section of the cerebellum and brain stem. Note the tremendous dilatation of the fourth ventricle and dilated foramen of Luschka and the granular appearance of the ependymal lining.

The liver appeared to be normal and weighed 690 Gm. On cut surface it presented the markings of chronic passive congestion. The gallbladder and bile ducts were normal.

The spleen was not enlarged and weighed 45 Gm. It was firm on section and showed normal markings.

The gastro-intestinal tract and pancreas showed no changes.

The kidneys were normal in size, each weighing 60 Gm. The capsule stripped with ease, leaving a smooth surface. Section revealed normal markings. The pelves, ureters and bladder were normal.

The sella turcica was flattened in the anteroposterior diameter and somewhat broadened laterally. The pituitary gland when removed showed similar antero-

posterior compression and measured 15 mm. in width, 10 mm. in the anteroposterior diameter and 7 mm. in height, not including the infundibular stalk. Horizontal section of the gland revealed no visible changes. The organ was fixed at once with Regaud's fluid.

The thyriod gland did not appear to be enlarged and weighed 7.5 Gm. Its capsule was smooth. On section the organ appeared reddish brown, firm and homogeneous and showed no visible colloid. There were no nodules in it.

The parathyroid glands could not be found.

The adrenal glands appeared to be normal, one weighing 10.5 Gm. and the other 13 Gm. On section, there were no visible changes.

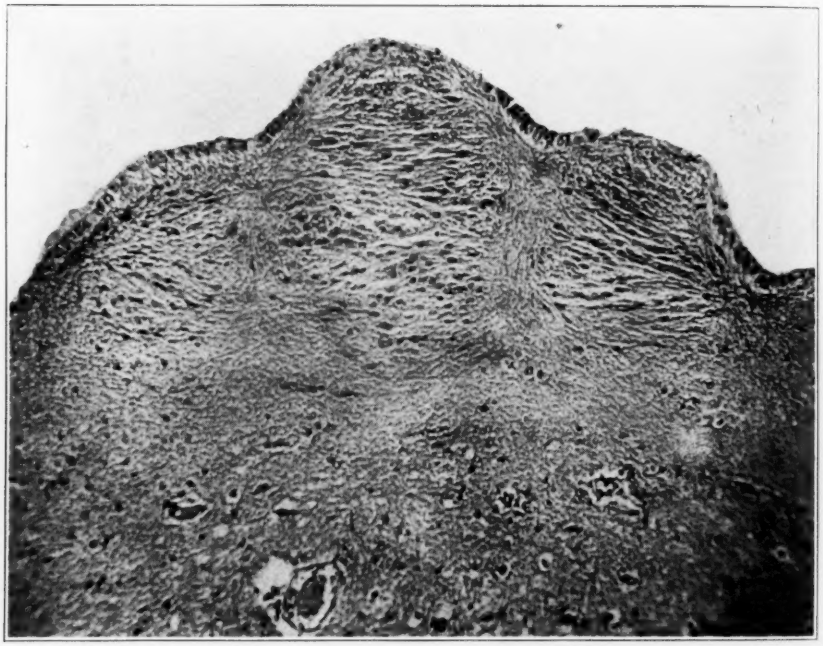

Fig. 5 (case 2).—Section showing ependymitis of the wall of the third ventricle. Note the destruction of the ependymal layer and the ependymal cells embedded in fiber proliferations. Hematoxylin and eosin stain.

The ovaries were enlarged, measuring 3.5 by 1.5 by 1 cm. Each had a firm grayish capsule. Cut section revealed discrete hemorrhagic areas varying from 0.5 to 2 mm. in diameter.

The vaginal mucosa was thickened; the cervix and uterus appeared virginal and normal. There was no evidence of bleeding of the endometrium.

The nipples were not raised above the surrounding skin; the glandular lobules and fat were abundant on section. There was no evidence of lactation.

Microscopic examination of the brain showed definite cortical atrophy and moderate edema. The small pineal remnants showed no abnormalities of cell outlines or staining characteristics.

Sections through the third ventricle and part of a lateral ventricle, stained with hematoxylin and eosin, showed a marked ependymitis in the third ventricle. This had an appearance similar to that found in dementia paralytica and evidently was chronic in nature.

The process was much more marked in the lining of the third ventricle than in the lateral ventricle, and no other distinctive pathologic process was seen except a condensation of brain tissue. There was no evidence of hemorrhage, tumor or encephalitis.

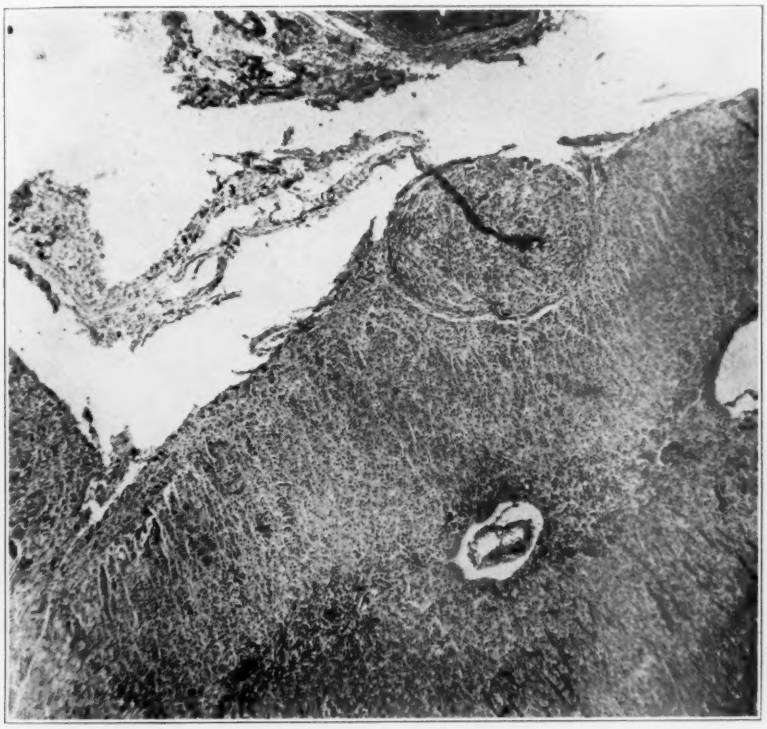

Fig. 6 (case 2).—Photomicrograph of the right adrenal gland, showing the cortical adenoma surrounded by otherwise normal cortical tissue.

In many areas the alveoli of the lungs were filled with an exudate consisting almost entirely of polymorphonuclear leukocytes. In other areas the exudate in the alveolar spaces consisted of polymorphonuclear leukocytes, red cells and pale homogeneous eosinophilic material, with little or no fibrin. An interlobular septum was seen to be infiltrated with polymorphonuclear leukocytes. Many capillaries in the alveolar walls were engorged with red cells. The pleura appeared edematous. In other sections bronchial mucosa was desquamated, and the bronchial lumina contained many leukocytes.

Serial sections of the pituitary gland were made in a horizontal plane and stained at intervals of from 20 to 60 microns. No foci of hyperplasia or tumor

formation was noted. The pars nervosa showed no invasion of epithelial elements. Unfortunately, postmortem autolysis had proceeded so far as to prevent accurate study of the various cell types by any of the various cytoplasmic stains. Application of the Mallory-Heidenhain aniline blue-acid fuchsin stain revealed no apparent disproportion in the distribution of alpha and beta cells. However, quantitative estimates were not made because of the autolysis.

The follicles of the thyroid gland appeared irregular in size and shape, but no infolding of the epithelial linings was seen. The colloid was excessive in amount and stained darkly eosinophilic and filled the distended follicles. The cells were of low cuboidal type. There was an increase in the number of lymphocytes and fibroblasts in the interstitial tissue. No foci of involution were found. One section showed parathyroid tissue, which appeared to be normal. One section

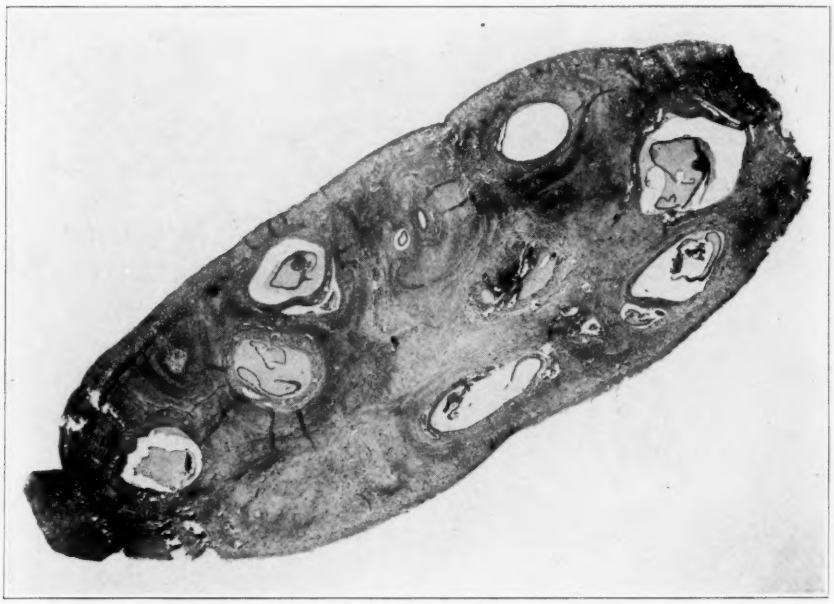

Fig. 7 (case 2).—Photomicrograph of a section of one ovary, showing mature and maturating graafian follicles and cyst formation.

of the adrenal glands showed a well circumscribed cortical nodule of cords of epithelial cells similar to those seen in the adjacent cortex. It was about one-fifth the size of a lower power field. Cortical tissue in general was increased in amount. Medullary tissue was scanty.

One ovary was divided in equal parts, and one-half was examined by Dr. Robert Frank. (Hormone studies were unsuccessful.) The other half was embedded in paraffin, and numerous sections were studied microscopically. The other ovary was divided, fixed in formaldehyde, and sectioned completely at levels of 20 microns. Sections of both ovaries revealed many follicles in various stages of maturation. No corpora lutea were found. There were large numbers of primordial follicles and a number of atretic follicles. The maturating follicles uniformly

showed degeneration of the theca interna, the cells being uniformly pyknotic and desquamated into the follicle lumen. Most of the follicles contained a moderate amount of bright pink eosinophilic homogeneous material. The ova were in various stages of degeneration in the maturating follicles. Many of the follicles were widely dilated, forming small cysts. No areas of hemorrhage were noted.

The cortex and medulla of the thymus were not differentiated. There was moderate deposition of adipose tissue. Hassall's corpuscles were large and fairly numerous. Scattered throughout were foci of coarse basophilic material.

Section through the breast showed normal overlying skin. The breast tissue contained a considerable amount of adipose tissue, fibrous tissue and well developed

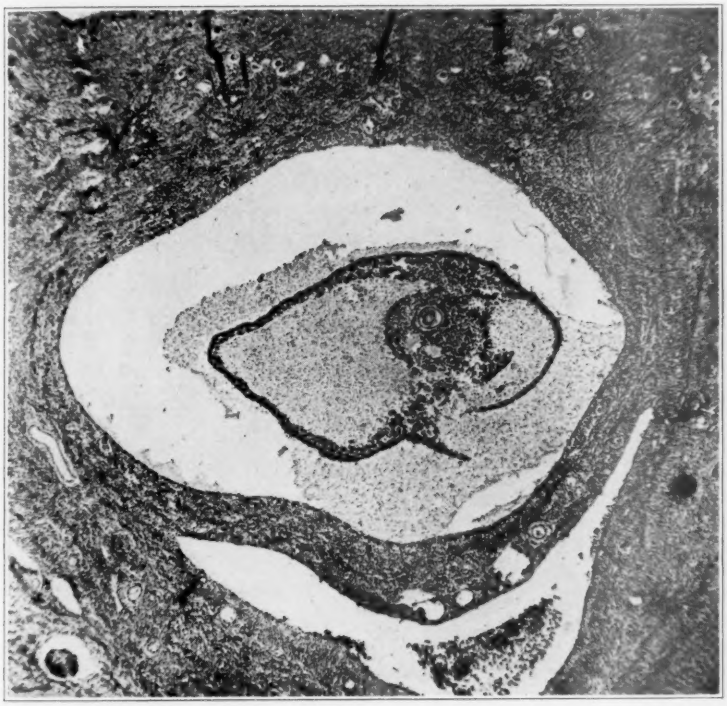

Fig. 8 (case 2).—Photomicrograph of a graafian follicle showing cystic dilatation, separation of the granulosa layer and degeneration of its cells. The intact ovum may be seen.

glandular nodules. The acini appeared large, and the epithelial linings were single layered throughout. In some acini a small amount of homogeneous eosinophilic material was seen.

Sections of the other organs, the myocardium, liver, spleen, pancreas and kidney, and a section of a costochondral junction showed no significant changes and confirmed the macroscopic diagnosis.

The final primary pathologic diagnoses were hydrocephalus internus, cortical atrophy with marked atrophy of the mamillary bodies, chronic ependymitis, sclerosis of the basal leptomeninges with adhesions to the dura and lobular pneumonia

The secondary diagnoses were: pubertas praecox with macrogenitosomia, physiologic hyperplasia of the breasts and ovaries, microcystic degeneration of the ovaries, chronic passive congestion of the liver, mild colloid goiter; miliary cortical adenoma of the right adrenal gland and moderate involution of the thymus with focal calcification.

COMMENT

The two cases presented resemble each other in that hydrocephalus and spastic paralysis were outstanding and each patient displayed precocious somatic development and precocious sexual development of the homologous type. We have based our conclusions on case 2 because of the benefit of necropsy observations.

The existence in these patients of hydrocephalus with its consequent train of paralysis and neurologic signs can be attributed to birth trauma and meningitis, respectively. The existence of the precocious hyperfeminization without evident menstruation, however, is more difficult to explain.

Although tumor of the adrenal cortex or hyperplasia may be associated with precocious sexual development in young males, it is manifested in females by the development of heterologous sex characteristics and not, as in our case, of homologous sex characteristics. The postmortem observation of a small cortical adenoma in our case does not alter the diagnosis, since such nodules are not infrequent in the course of a postmortem examination, and as such they have no significance. Another pathologic state which could be ruled out in the clinical diagnosis was that due to ovarian tumor.[12] Arrhenoblastoma is generally associated with symptoms similar to those seen with lesions of the adrenal cortex, namely a defeminization or masculation. The existence of a granulosa cell tumor of the ovary (in case 2) was considered as the most likely condition in our patient, since hyperfeminization was outstanding. However, physical examination revealed no adnexal masses, and adequate sections of both ovaries revealed no hyperplasia or new growth of granulosa cells to account for the precocity. The absence of any known pathologic changes in the ovaries or the adrenal glands indicates a different etiologic basis for our patients.

The one outstanding feature common in our cases and in most of those culled from the literature is hydrocephalus. Certainly, hydrocephalus as commonly observed is not associated with an endocrine disturbance and cannot be considered in itself significant in the development of sexual precocity.

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12. Novak, E., and Long, J. H.: Ovarian Tumors Associated with Secondary Sex Changes, J. A. M. A. **101**:1057 (Sept. 30) 1933. Meyer, R.: Pathology of Some Special Ovarian Tumors and Their Relation to Sex Characteristics, Am. J. Obst. & Gynec. **22**:697 (Nov.) 1931.

Kraus,[13] however, has recently contributed observations on the rôle of increased intracranial pressure in relation to disturbances of the pituitary gland, which can be applied to these cases. Kraus expressed the opinion that in patients with neoplasm of the brain or meninges, or in patients with chronic internal hydrocephalus associated with a chronic increase in intracranial pressure, the anterior lobe of the pituitary gland becomes either underactive or overactive, depending on the particular changes that had occurred in the hypothalamic region.

When there was actual destruction or necrobiotic changes of the hypothalamic region, causing the hypothalamic-infundibular-hypophysial chain to be broken, Kraus observed the following picture: The pituitary gland was found to be either normal or lighter in weight than normal and correspondingly normal or underactive in function. There were retrogression of sexual characteristics, diminution of libido sexualis and dwarfism in the young. At the same time, obesity and diabetes insipidus occurred in some instances, presumably through a disturbance of the nervous pathway of the hypothalamic-hypophysial system.

When the hypothalamic-infundibular-hypophysial chain was not broken and when there were no necrobiotic changes in the infundibular stalk, even when the floor of the third ventricle and the hypothalamus were paper thin from compression, Kraus claimed that the following effects were noted: The pituitary gland was found usually to be above normal in weight and showed hyperplasia of all the three types of cells of the anterior lobe of the pituitary gland. Menstrual disturbances and diminished libido were present in some of the cases, although spermatogenesis in most of the males was not disturbed.

In addition to the enlargement of the pituitary gland, the ovaries in 83.3 per cent of Kraus' patients with increased intracranial pressure showed microcystic degeneration. Furthermore, on examination of the blood and urine of these women, it was found that the follicle-stimulating component was increased in amount in 60.3 per cent of the women. (Several of the males also showed this increase in follicle-stimulating substance.) It was further noted that on injection of the urine of such patients into female animals, a ripening of the follicles was produced, and in some the same microcystic degeneration of the ovaries was reproduced. The Ascheim-Zondek reaction was observed in various

13. Kraus, E. J.: The Hypophysis and Ovaries in Chronic Intracranial Pressure, Med. Klin. **27**:547 (April 10) 1931; Zur Genese der Kleincystischen Degeneration der Ovarian, Arch. f. Gynäk. **152**:383, 1933; Prolan Excretion in Chronic Increased Intracranial Pressure, Klin. Wchnschr. **11**:1577 (Sept. 17) 1932; Changes in the Hypophysis in Chronic Increased Intracranial Pressure, Ztschr. f. d. ges. Neurol. u. Psychiat. **146**:548, 1933; Neurobiotic Changes in the Hypophysis, Especially in the Stalk, Virchows Arch. f. path. Anat. **290**:658, 1933.

degrees, from a simple enlargement of the follicles to a markedly positive reaction, I, and in some instances to a positive reaction, III.

Although the actual connection between chronic increased intracranial pressure and microcystic degeneration of the ovaries is uncertain, Kraus expressed the opinion that the morphologic and biologic changes which occurred in these ovaries could be attributed to the hyperplasia of the anterior lobe of the pituitary gland.

Correlating Kraus' findings with our own, it can be seen that in our case 2 there were (1) chronic increased intracranial pressure, without a neoplasm, as a consequence of the internal hydrocephalus; (2) a thinned and atrophic hypothalamus but an apparently intact hypothalamic-hypophysial pathway; (3) a somewhat enlarged and compressed pituitary gland with an apparently normal histologic structure; (4) evidence of much follicle maturation without luteinization in the ovaries, and (5) notable cystic formation in the ovaries. The last cannot be evaluated because of the absence of data dealing with frequency and specificity of this change in precocity as distinct from normal prepubertal states.

It is possible, therefore, by applying Kraus' findings, to arrive at a possible explanation for the type of precocity noted in these cases. It is suggested that there was overactivity of the pituitary gland due in some yet to be explained manner to chronic increased intracranial pressure without neoplasm and with no apparent disruption in the hypophysial-hypothalamic pathway. It is also suggested that the changes in the ovaries noted in case 2 were due to the follicle-stimulating component of the overactive pituitary gland, because the changes were similar to the microcystic changes noted in Kraus' work. It is further suggested that the follicular hormone presumed to be produced through the ripening of the ovarian follicles was probably responsible for the early ripening of the accessory and secondary sex characteristics.[14]

SUMMARY AND CONCLUSION

Several cases from the literature are reported as examples of pubertas praecox and macrogenitosomia praecox in males and females, with and without menstruation in the females, without any apparent lesions in the endocrine glands which one usually associates with precocity.

The findings are reported in the cases of two young girls who showed a similarity of symptoms, such as chronic internal hydrocephalus, spastic paralysis and macrogenitosomia praecox without menstruation. One of these cases was studied at necropsy.

14. Allen,[10] pp. 412-417.

In addition to the existing hydrocephalus, pathologic studies of the ductless glands showed a normal pineal gland, one normal parathyroid gland, inconsequential involvement of the thyroid and adrenal glands, an enlarged, somewhat compressed pituitary gland and many follicle cysts in the ovaries. The follicles were in various stages of maturation, but none exhibited luteinization.

It is suggested that chronic increased intracranial pressure with compression of the hypothalamic-infundibular-hypophysial pathway was the starting point for the development of the precocious state.

Dr. Benjamin Kramer, chief of the Pediatric Department, and Dr. Benjamin E. Wolfort and Dr. Joseph E. Milgram, of the Orthopedic Department of the Brooklyn Jewish Hospital, gave us permission to study and to include case 1 in this report.

Dr. Douglas Symmers, director of the Pathologic Laboratories of Bellevue Hospital, gave us permission to report the pathologic data in case 2. The report of the examination of the brain was made by Dr. Lewis Stevenson and the histologic studies of the pituitary gland and ovaries by Dr. Irving Graef.

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INTESTINAL STASIS DUE TO LOW MINERAL INTAKE

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About two years ago, in the course of some other experiments, it was noted that rats fed a diet low in minerals showed intestinal stasis,[1] and this condition has been extensively studied since that time.

TABLE 1.—*Composition of the Diets*

	Adequate Diet, Percentage	Diet Deficient in Minerals, Percentage
Corn starch	60	64
Purified casein	18	18
Hydrogenated oil	10	10
Cod liver oil	2	2
Dried brewer's yeast	6	6
Osborne and Mendel's salt mixture	4	..

TABLE 2.—*Analysis of Diets*

	Adequate Diet, Percentage	Diet Deficient in Minerals, Percentage
Total ash	3.3	0.8
Calcium	0.43	0.08
Potassium	0.53	0.03
Phosphorus	0.33	0.12

EXPERIMENTS ON RATS

Litters of rats which had just been weaned were divided into two groups. One half of each litter was fed an entirely adequate diet, and the other half was fed a diet low in minerals but otherwise complete. The composition of the two diets is shown in table 1, and it is evident that both of them contained sufficient carbohydrate, good protein, fat and vitamins A, D and B complex. It is not necessary to feed any vitamin C, as the rat can synthesize this substance. The Osborne and Mendel salt mixture [2] contains reasonable amounts of all the essential minerals except copper, which was, however, present in the rest of the diet. The rats were given distilled water only to drink.

If the two diets are ashed, the ration deficient in minerals contains about 0.8 per cent ash and the adequate diet about 3.3 per cent ash (table 2). The

From the Department of Pediatrics, University of Toronto, and the Hospital for Sick Children, Toronto, under the direction of Dr. Alan Brown.

Read at the Forty-Eighth Annual Meeting of the American Pediatric Society in Joint Session with the Canadian Society for the Study of Diseases of Children, Bolton Landing, N. Y., June 11, 1936.

1. Robertson, E. C., and Doyle, M. E.: J. Nutrition **9**:553, 1935.
2. Osborne, T. B., and Mendel, L. B.: J. Biol. Chem. **37**:572, 1919.

adequate diet contains about five times as much calcium and about eighteen times as much potassium as the deficient diet.

After the rats had been fed these diets for four weeks or more, they were killed and their intestinal tracts were examined (figure 1). In the rats fed the deficient diet the colons were distended and contained much more fecal material than those of the rats fed the adequate diet. The walls of the colon were also thinner in the rats fed the deficient diet. The cecum, which is a stomach-shaped organ in the rat, was usually more dilated also and contained more material in the rats fed the deficient diet, and the lower part of the ileum showed the same dilatation and overloading. These findings were confirmed by weighing the intestines and their contents.[1] Apparently the rats fed the deficient diet suffered from atonic constipation.

Microscopic sections of the intestines showed no actual lesions in the muscle but did show definite thinning of the muscle layers in the cecum and colon, as if

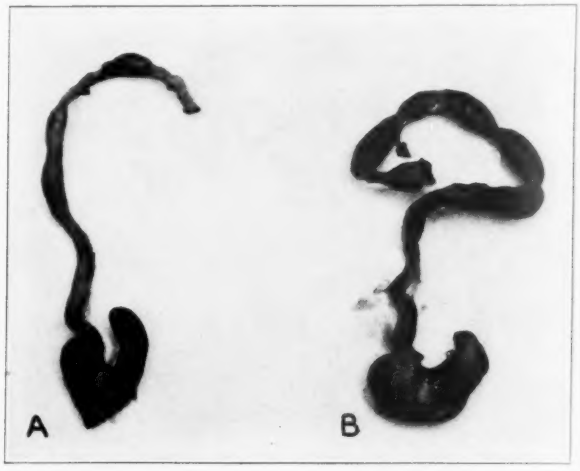

Fig. 1.—*A*, photograph of the large intestine of a rat fed an adequate diet, and *B*, of a rat fed a diet deficient in minerals. Both animals weighed 60 Gm. Note the dilatation and overloading of the colon (upper part) and cecum (lower part) of the rat fed the deficient diet.

the muscles had lost their tone and become stretched by the masses of fecal material. These findings fitted in well with the later results.

In order to demonstrate this stasis or constipation in living rats, groups of them that had been fed the two diets for four weeks or more were given a small constant dose of carmine, and then the feces were collected daily and examined for carmine. Each rat had a separate cage, and the feces were collected on paper placed below the floor. After the carmine was fed, the rats fed an adequate diet passed bright red feces for three or four days. The rats fed a deficient diet, however, passed paler red feces for longer periods, as if the concentration of carmine in the feces was less. It was found that the only way to be sure if carmine was present in the feces was to examine a suspension of it under the microscope. Microscopically the carmine showed up as bright red sharp-edged crystals in the midst of the brown fecal material. This method was thoroughly checked, and it proved reliable.

The results of one of these experiments are shown in figure 2. The higher the column, the longer the carmine was present in the feces. If the column is solid, the carmine could be seen definitely with the naked eye; if it is hatched, the carmine was seen only under the microscope. Except for the first three days, all the specimens were examined microscopically. The eight rats fed the adequate diet excreted carmine for only from three to seven days; those fed the deficient diet excreted it for from twelve to twenty-one days. These results were confirmed in at least two hundred other rats.

It was also found that the stasis caused by the deficient diet could be cured by feeding the rats the adequate diet for four weeks, as is shown in figure 3. These three rats, which showed marked stasis when on the deficient diet, were fed the adequate diet for four weeks and were then given carmine again. They now showed no stasis at all. It would appear, therefore, that the stasis was functional and could be relieved by feeding the missing minerals.

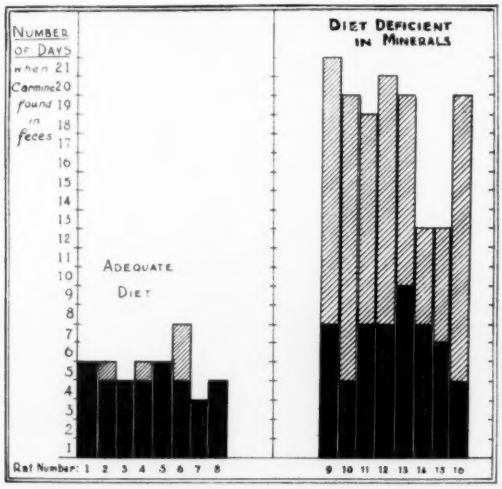

Fig. 2.—Chart showing the much slower excretion of carmine by rats fed a diet deficient in minerals as compared with that by rats fed the adequate diet. The solid column represents the carmine that could be seen with the naked eye and the hatched column, that which was observed only under the microscope.

Rats on these diets were also fed small constant amounts of barium sulfate, and the feces were collected daily and set up in wooden trays, which were divided into horizontal troughs. The feces of one rat were put in one horizontal trough, the daily lots being separated by the small vertical wooden partitions. The feces were collected the day before the barium was fed, and these were put on the right side of the row as a control. Roentgenograms were then made of the tray containing the feces. Figure 4 is a roentgenogram of the feces passed twenty days after a barium sulfate meal by a rat fed the diet deficient in minerals. Three rows of the tray were used in this case merely for the sake of the shape of the picture. The feces collected before the barium was fed (lower right corner) look very pale as compared with the other feces, all of which contain barium. The barium appears black in this positive print. In order to check the roent-

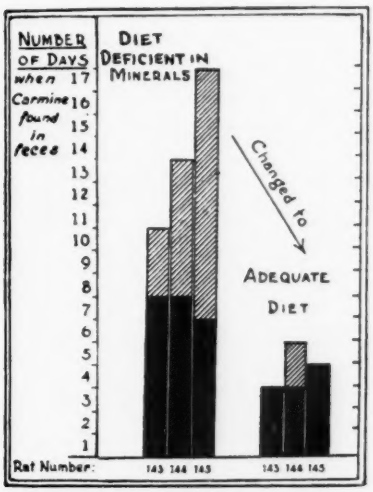

Fig. 3.—Chart showing stasis caused by a diet deficient in minerals and its cure by the feeding of an adequate diet. The solid and hatched areas have the same indications as in figure 2.

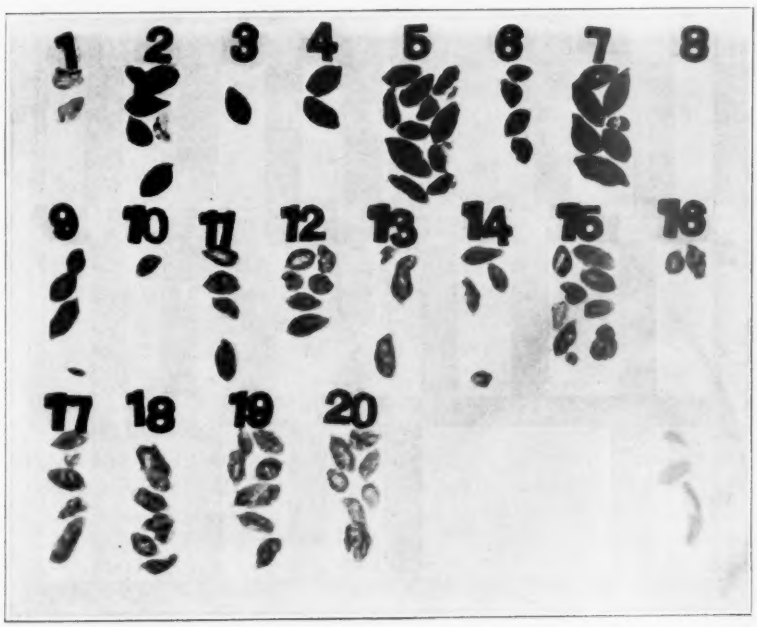

Fig. 4.—Roentgenogram of the feces passed by a rat fed a diet deficient in minerals after a barium meal. Barium was present in the feces for twenty days. Control feces, collected before the barium meal, are shown in the lower right corner (no number).

genographic findings, the feces passed on the twentieth day were analyzed for barium and it was found that they contained a great deal. It is evident that the rat was passing a small amount of feces daily.

Figure 5, a similar roentgenogram, shows the much larger amounts of feces passed by the corresponding rat fed the adequate diet. Barium was present for five days according to the roentgenogram. On chemical analysis a moderate amount of barium was present in the feces on the fifth day and a slight amount on the sixth. After the sixth day, no barium was found. Similar tests were carried out in two hundred and twenty-eight rats, and the results are shown in table 3. The rats fed the diet deficient in minerals excreted barium on the average for ten and six-tenths days; those fed the adequate diet, for four and four-tenths days. The rats fed the deficient diet showed more variation, as is evident by the larger standard deviation, but the difference between the two groups of rats was highly significant statistically.

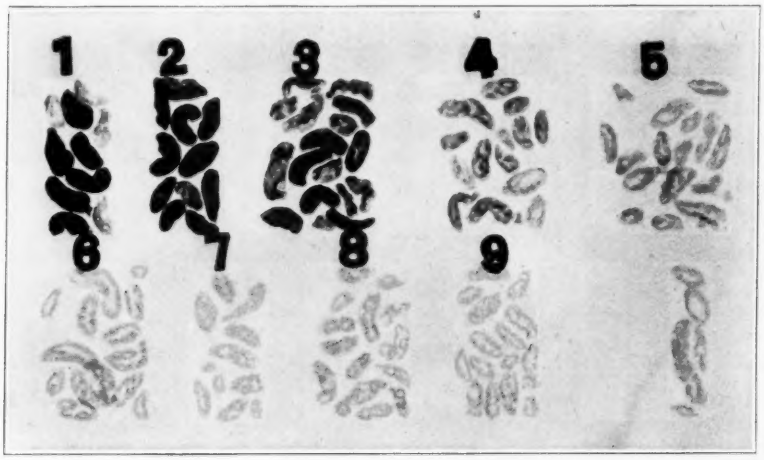

Fig. 5.—Roentgenogram of the feces passed by a rat fed an adequate diet after a barium meal. Barium was present for five days. Control feces, collected before the barium meal, are shown in the lower right corner (no number).

Various elements were added to the diet deficient in minerals to see if stasis could be prevented. Rats were fed the five diets shown in table 4. One per cent of potassium carbonate and 1 per cent of calcium carbonate were used because the adequate diet contained corresponding amounts of potassium and calcium. The figures given represent the average number of days that barium was present in the feces, and about one hundred rats were used to get each average. The rats fed the diet deficient in minerals of course showed stasis. When 1 per cent of potassium carbonate was added to the deficient diet there was a slight decrease in stasis, but it was still quite marked, and if the amount of potassium carbonate was raised to 2 per cent the results were the same. When 1 per cent of calcium carbonate was added, there was only slight stasis. Unfortunately, when the diets were supplemented with either potassium or calcium carbonate the results were somewhat variable. When both potassium and calcium carbonate were added together, there was again only slight stasis, and the results were very consistent.

The calcium and potassium together were therefore almost as effective as the complete salt mixture, and the calcium is apparently the more important factor.

It was also found that when stasis was present the material in the cecum and colon was much more acid (table 5). The intestinal p_H also has no relation to the reaction of the food.

EFFECTS OF FEEDING A DIET LOW IN CALCIUM AND POTASSIUM TO CHILDREN

Since the addition of calcium and potassium will prevent stasis, it seemed possible that a deficiency of these two elements might cause

TABLE 3.—*Period of Excretion of Barium*

	No. of Rats	Barium in Feces, Days	Standard Deviation
On diet deficient in minerals	117	10.6	±4.1
On adequate diet	111	4.4	±1.4

TABLE 4.—*Average Number of Days Barium Was Present in Feces*

Diet Deficient in Minerals	Deficient Diet + 1% K_2CO_3	Deficient Diet + 1% $CaCO_3$	Deficient Diet + 1% K_2CO_3 + 1% $CaCO_3$	Adequate Diet
10.6	8	5.1	4.7	4.4

TABLE 5.—*Hydrogen Ion Concentration of the Large Bowel*

	Diet Deficient in Minerals	Deficient Diet + 1% K_2CO_3	Deficient Diet + 1% $CaCO_3$	Deficient Diet + 1% K_2CO_3 + 1% $CaCO_3$	Adequate Diet
Cecum	6.1	6.2	6.9	6.9	7.0
Colon	6.2	6.1	6.9	7.0	7.0
	Stasis	Considerable stasis	Little stasis	Very little stasis	No stasis

stasis, and it was decided to try out the effect of a diet containing about 0.2 Gm. of calcium and about 1 Gm. of potassium daily on convalescent children from 7 to 12 years of age. In other words, the intake of these minerals was reduced to about one fifth of the commonly accepted optimum.

The main restriction was that no milk was given, but 2 ounces of 16 per cent cream diluted with water was substituted. The diet was palatable and included varying combinations of the following foods: white bread and various finely milled cereals, rice, tapioca, macaroni, grapefruit, oranges, lemons, apples, apricots, pears, grapes, blueberries, bacon, eggs, meat, fish, chicken, gelatin, twice-cooked potatoes, carrots and asparagus and small servings of lettuce and butter. The daily ash was calculated on two representative daily menus and was found to be 4.5 and 5.1 Gm., or 0.8 and 1.1 per cent, respectively. In a third menu the ash was found to be 0.8 per cent on calculation, and 0.86 per cent on ashing. Two regular

hospital menus for similar children contained 12.98 and 14.16 Gm., or 1.7 and 1.9 per cent, of ash, respectively.

The diet low in calcium and potassium contained from 2.8 to 4.5 Gm. of fiber per day, which was somewhat lower than the amount in the regular hospital diet, which was from 4.6 to 8 Gm. For two of the children 2 Gm. of powdered ash-free filter paper was added to the diet low in ash, which raised the amount of fiber to between 4.8 and 6.5 Gm. daily, but the children became constipated nevertheless. According to Cowgill and Anderson,[3] from 90 to 100

TABLE 6.—*Percentage of Days on Which Children Had No Bowel Movement*

Child	During Four Weeks on Usual Ward Diet	During Four Weeks on Diet Low in Ca and K
J. H.	8	36
B. W.	8	40
E. C.	0	41
L. B.	23	33
S. B.	20	39
A. W.	0	33
R. M.	11	48
E. E.	7	64
J. B.	7	24
L. C.	Not determined	No movement without enema
N. B.	26	50
B. A.	28	46
B. C.	21	50
K. S.	0	57
A. S.	11	20
E. J.	0	3
J. M.	6	6
B. M.	Not determined	0
G. E.	0	0

TABLE 7.—*Number of Days Barium Remained in the Appendix* *

Child	No. of Days Barium Remained in the Appendix		
	Diet Low in Ca and K	Adequate Diet	Normal Diet
K. S.	19	1	0
B. A.	5 (last plate taken)	0	—
E. E.	4 (last plate taken)	1	1
L. C.	6	—	—
L. B.	13	—	—
E. J.	4	—	1

* The dash indicates that no determinations were made.

mg. per kilogram of body weight is the minimum intake of fiber for adults. These children weighed on the average about 34 Kg. and would at that rate need about 3.1 Gm. of fiber. Most of the diets low in ash contained this much or more.

Within from five to ten days after the children were put on this diet they usually began to have less frequent bowel movements. No laxatives or enemas were given during the test, which lasted approximately four weeks. Table 6 shows the percentage of days on which the children had no bowel movements

3. Cowgill, G. R., and Anderson, W. E.: Laxative Effects of Wheat Bran and "Washed Bran" in Healthy Men: Comparative Study, J. A. M. A. **98**:1866 (May 28) 1932.

when fed the usual ward diet and when fed the diet low in calcium and potassium. Five of the children had practically daily movements while on each diet, but the other fourteen, or 74 per cent, showed constipation.

After the children had been fed the diet low in calcium and potassium for from three to four weeks, and while they were still on it, they were given a barium sulfate meal. Roentgenograms of the abdomen were taken daily. A number of the children were given a preliminary barium meal while on their usual ward diet, and roentgenograms were taken daily. Six of twelve children so examined were much slower in getting rid of the barium from their intestinal tracts (from six to twenty-eight days) when on the diet low in ash than when on the normal diet (from two to four days).

Fig. 6.—Roentgenogram of the abdomen of K. S. taken when on a diet low in calcium and potassium, nineteen days after a barium meal. The appendix contains much barium.

Of eighteen children fed a barium meal while on the diet low in calcium and potassium, six, or 33 per cent, retained the barium in their appendixes for from four to twenty-one days. These results are shown in table 7. Figure 6 is a roentgenogram of the abdomen of K. S., taken when she was on the diet low in calcium and potassium, nineteen days after the barium meal. The appendix contains a great deal of segmented barium, which in this "positive" print appears black.

Some of these same children were given 0.8 Gm. of calcium in the form of calcium lactate and 5 Gm. of potassium in the form of potassium chloride in

addition to the diet low in ash, and the diet was then known as the adequate diet. Neither of these salts is thought to be laxative. The first three children (table 7) were fed the adequate diet for three weeks and then given another barium meal. No barium was seen in the appendixes after the first twenty-four hours. Figure 7 is a roentgenogram of the abdomen of K. S., when she was on the adequate diet, taken two days after the barium was fed. No barium is seen in the appendix. In two of these three children the addition of minerals caused more regular bowel movements.

Three of the children when on the normal ward diet did not retain the barium in their appendixes for more than one day (table 7). This test could not be carried out on the other children because they were discharged from the hospital.

Fig. 7.—Roentgenogram of the abdomen of K. S. taken when on an adequate diet two days after a barium meal. No barium was seen in the appendix.

The first child (K. S.) mentioned in table 7 was given the extra calcium and potassium nineteen days after the barium meal, when the appendix still contained barium. Much less barium was seen in the appendix on the next day (twentieth), but the barium was not all out of the appendix until two days later. The fourth child (L.C.) was given the extra calcium and potassium after the barium had been retained in the appendix for six days. The barium remained in the appendix for three days more, but on the fourth day it was gone. Whether the addition of the minerals hastened the expulsion of the barium from the appendix is therefore uncertain.

The tests on children are not completed, but they suggest that diets low in calcium and potassium are constipating and that such diets low

in ash may cause stasis in the appendix which might easily increase the chances of formation of fecaliths and infection.

CONCLUSIONS

Rats fed a diet low in minerals show intestinal stasis, which is evident by dilatation and overloading of the large intestine and by much delayed excretion of carmine and barium. The stasis can be cured by adding the missing minerals.

When calcium and potassium salts are added to diets deficient in minerals, practically no stasis is found.

The contents of the large intestines are definitely more acid in rats showing stasis than in the controls.

Nineteen children were fed diets low in calcium and potassium. Fourteen of these showed constipation.

When given a barium meal, 33 per cent of eighteen children fed diets low in calcium and potassium retained the barium in the appendix for abnormally long periods (from four to twenty-one days). The same children when fed normal diets did not show barium in the appendix for more than one day.

MYRINGITIS BULLOSA HAEMORRHAGICA

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The severity and frequency of serious complications of the otitic infections accompanying influenza have impressed many physicians, so that even now when bullous hemorrhagic lesions are seen on the ear drum or on the otitic canal wall a feeling of considerable concern is aroused. After seeing many such complications in persons with non-influenzal conditions, I was impressed by the sudden and severe onset and by the intensity of the associated pain, but also by the favorable outcome in most instances. I attempted, therefore, to learn through the literature and by personal communication with competent otologists what the general opinion is as to the significance of these lesions, their course and the therapy of choice, and I was surprised at the differences in the opinions expressed. Some regarded these lesions as a sign of the presence of true influenza; others expressed the belief that they occur in the same manner in which herpes labialis may occur with numerous and varied infections, and still others stated that otitis media is always associated with this condition. Some were conservative in their therapy and recommended watchful waiting, while others were more concerned and urged prompt surgical intervention, at least rupturing the bullae, and often myringotomy.

The inconsistencies of the common impressions of the import of this otitic disturbance and its therapeutic implications in noninfluenzal patients led me to make detailed records of a series of such cases to learn what I could of their clinical course. I started with the preconceived idea that I would not interfere with the course of these lesions unless the indications for surgical intervention were beyond question, even to the conservative otologist.

From Jan. 1, 1934, to June 1, 1936, I was able to follow eighty-seven patients with myringitis bullosa haemorrhagica from the first day of the illness to its conclusion. The patients were all from private practice among white children of comfortable homes.

Total.....	87	Bilateral.....	56	Left ear.....	15	Right ear.....	16
Males	48						
Females ..	39						

The condition recurred in nine children within a period of from two weeks to one year. In six families it occurred in two children simultaneously or started a few days apart.

LOCATION AND CHARACTER OF LESIONS

Forty-five of the ears had bullae on the canal wall or on both the canal wall and the drum. Ninety ears had bullae primarily on the drum. Forty-seven of the ears had bullous lesions filled with serous fluid.

Data Concerning Eighty-Seven Cases of Myringitis Bullosa Haemorrhagica

Relation to Tonsils

Patients with tonsils in	58
Patients with tonsils out	29

Age Incidence

Under 1 year	2
1	4
2	9
3	12
4	8
5	13
6	11
7	8
8	7
9 and 10	5
11 to 14	6
20	1
30	1

In more than half of the cases the myringitis occurred between 3 and 6 years of age.
In more than two thirds the myringitis occurred between 2 and 8 years of age.

Conditions Which Were Complicated by Myringitis Bullosa Haemorrhagica.

Chickenpox	1
Mumps	1
Pertussis	3
Scarlet fever	4
Measles	3
Tonsillitis	10
Asthma	1
Sinusitis	3
Bronchitis	3
Pneumonia	3
Grip	6
Purpura	1
Otitis media	4
Acute infection of the upper respiratory tract	44

Seasonal Occurrence of Blebs

	1934	1935*	1936
January	9	3	7
February	1	2	7
March	10	2	7
April	3	2	4
May	5	2	4
June	1	0	1
July	1	0	..
August	0	0	..
September	1	0	..
October	2	0	..
November	6	2	..
December	1	4	..

* Note the relatively low incidence in 1935.

One hundred and three of the ears had bullous lesions which were serosanguineous or had become so within the first twenty-four hours after onset.

OUTCOME

One hundred and twenty-nine ears (90 per cent) in seventy-five children healed spontaneously. Fourteen ears in twelve children, or 10 per cent, showed purulent otitis media which in from eight hours to

fourteen days after the onset of symptoms began to discharge either spontaneously or after myringotomy. Mastoiditis with recovery after operation occurred three times in two children. One child, who had had myringitis bullosa haemorrhagica for the previous three consecutive years, with resulting purulent otitis media each time, died of meningitis after the fourth attack. At operation the mastoid bone was sclerosed but showed no evidence of acute infection. In 90 per cent of the cases the condition healed in one of the following ways:

	Instances
Bullae dried without rupturing	38
Bullae ruptured, then dried	42
Bullae disappeared after the fluid was absorbed	28
Bullae dried in distended condition, becoming brittle, the condition lasting from 14 to 20 days	3
Bullae ruptured, others dried and still others may have been absorbed	17

Among the 14 ears in which the involvement ultimately went on to purulent otitis media all had had bullae which ruptured spontaneously.

BACTERIOLOGY

Attempted culture of a virus from the fluid withdrawn from the blebs in seven cases failed each time. This was done by Dr. J. Goldman. No specific organism was found.

SYMPTOMATOLOGY AND COURSE

Pain and Tenderness.—The pain in the ear was unusually sharp and severe and frequently involved the periaural area in addition to the affected ear, sometimes extending over the entire side of the head. The pain lasted from four hours to four days, in a few instances seven days and once ten days. In the majority the pain was severe for from four to twelve hours, after which it seemed to subside spontaneously when the blebs had become larger, as if the formation of blebs numbed the drum and the canal wall. In several cases after the acute pain subsided noises were experienced, such as bubbling, crackling and those made by the rushing of water.

The pain was only partly relieved by the application of external heat, by the instillation of warm glycerin or by taking salicylates or aminopyrine. Codeine in large doses alone or with salicylates did relieve the pain in most instances. In some the pain continued unabated for days, and in these either there were fresh blebs or purulent otitis media developed. When the latter occurred, the pain was not entirely relieved either by spontaneous rupture of the drum or after paracentesis. Lying on the affected side or chewing frequently increased the discomfort. Headache was relatively common, and dizziness was experi-

enced by several. Periaural tenderness was present in all but twenty-three cases. This tenderness extended to half of the scalp in few, and in some pain was present in the supra-orbital region, causing these children to complain of pain over the eye. The periaural tenderness varied with the degree to which the wall of the canal was involved, being more severe the more extensively the canal wall was affected. It was less severe when the drum alone was involved. In some instances the tenderness was difficult to distinguish from true tenderness of the bone over the mastoid. Tugging of the auricle was painful in most cases early in the course of the disease.

Hearing.—In addition to the twelve in whom purulent otitis media developed, twenty-four children had diminution of hearing. Thirty-six had diminution of hearing from one to ten days. In only twelve of these did purulent otitis media develop. Hearing was affected most when the entire drum was involved, when the canal was occluded by blebs or when the canal and the drum were both extensively involved. The latter type of involvement progressed to otitis media most often.

Fever.—Fever usually occurred as part of the entire illness with which the bullous lesions were associated. In some cases there was no fever, whereas in others the temperature remained elevated to various levels from 100 to 104 F. for from one to seven days. Those patients in whom the original infection had cleared but in whom the myringitis continued in severe form had fever due to the myringitis. In this group those whose temperature rose to more than 102 F. for more than four or five days usually had purulent otitis media later, although in a few the fever continued for six or seven days without the spontaneous or surgical opening of the ear drum. In the latter group, which was small, I believe that it was fair to assume from the appearance of the drum that acute otitis media was present. In cases in which there was no fever or very little for one day the symptoms were usually mild and of short duration, and spontaneous healing occurred rapidly.

Duration.—In the majority of cases the bullae lasted three or four days, although all extremes from eight hours to fourteen days were represented in this series. In two cases involving three ears there was evidence of pathologic change for seventeen days. In these the bullae were without symptoms and were found to have dried without shriveling or losing their color. When touched with a curet these blebs broke as if they were dry casts of the bullae.

In one boy the bullae on the canal wall produced such extensive infiltration of the tissue that the canal seemed to have been closed off by what looked like an abscess of the canal wall. The pain and fever continued for ten days and were severe. Healing was spontaneous and without complication. The duration of the illness could not have

been predicted in most cases. In those, however, in which few or small lesions appeared on the drum only, the course was usually short, from twenty-four to sixty hours. In like manner, it might have been predicted that in those in which there was extensive hemorrhagic involvement of both the drum and the canal wall the condition would last a considerable time and that the possibility of the development of purulent otitis media would be greater.

Appearance of the External Ear.—In a few instances the pinna became red. In many the canal wall became red or crinkled prior to the appearance of bullous lesions, but the reddened area was not necessarily the site on which the bullae appeared.

In no instance were herpetic lesions noted on the external ear, and in none was there any herpes labialis. In one adult who had this condition the hemorrhagic blebs appeared on the external ear on the auricle.

When the blebs ruptured, serous or serosanguineous fluid appeared on the external ear and could usually be found on the pillow. The flow continued in some instances, being free for a day or two. When this occurred, the condition usually went on to purulent otitis media.

TREATMENT

The treatment employed was almost entirely limited to the alleviation of pain. External heat provided by a hot water bag or an electric heating pad was of some help. Salicylates and codeine in fairly large doses were of definite and considerable aid. Warm irrigations were usually painful and of no demonstrable use. Cleaning the canal with dry cotton was found to be irritating, often causing the appearance of a hemorrhagic bleb at the site of the friction.

Large wet dressings applied to the side of the head involved were comforting in many cases, especially when there was extensive periaural pain and tenderness.

Rupture of the blebs was not attempted in any case. Myringotomy was performed only when a bulging drum membrane associated with pain and fever was seen. Otherwise surgical intervention was not undertaken.

SUMMARY

Myringitis bullosa haemorrhagica was seen in my practice in eighty-seven children in twenty-nine months, from Jan. 1, 1934, to June 1, 1936. In most cases the involvement occurred in the late fall, winter and early spring. It was more common in boys. It occurred bilaterally twice as often as unilaterally. It recurred in nine children in from two weeks to a year after the first attack. It occurred simultaneously

or within a few days in two siblings in six families. It was observed twice as often in children who had not had their tonsils and adenoids removed as in those who had had this operation.

While all ages from 6 months to 14 years were represented in this group (also two adults), half of the patients were between 3 and 6 years of age and two thirds of them were between 2 and 8 years of age.

The conditions which this type of myringitis complicated were largely acute infections of the upper respiratory tract and tonsillitis. Measles, pertussis, scarlet fever, sinusitis, bronchitis, pneumonia, grip or otitis media was present in most of the other cases. True influenza was not observed among these patients or during the time of the occurrence of the myringitis, although no culture for the influenza bacillus was made.

The bullous lesions appear most commonly on the drum and most often are hemorrhagic or become so within the first twenty-four hours of the illness.

Lesions involving the drum and canal or those with extensive involvement of the drum alone are associated with more severe and more persistent pain and are more likely to go on to purulent otitis media.

The latter are also associated with greater periaural tenderness and with diminution of hearing.

The diminution of hearing does not necessarily mean that purulent otitis media is present.

COMMENT

The observations recorded indicate that myringitis bullosa haemorrhagica associated with the ordinary infections of the respiratory tract is a different condition, a much milder one, than that reported as a complication of true influenza. The serious complications noted with the latter were rarely seen in my group of cases. I doubt whether anything can be gained by incising the blebs and am certain that myringotomy, unless the usual indications for this procedure exist, is useless.

The lesions do not impress me as being similar to those of herpes labialis. In contrast to the lesions of herpes, they are painful, commonly are hemorrhagic and may occur with the mildest type of infection of the upper respiratory tract; in no instance were these lesions and herpes labialis present simultaneously.

The fact that in all cases an infection of the upper respiratory tract was present suggests that the pathway of otitic involvement was

through the eustachian tube, first causing inflammation of the middle ear and secondarily the bullous myringitis. Yet the evidence that this is so is not convincing.

Thus, from the results obtained by conservative treatment in this group, I believe that otitis media could not have been present in all the cases. There were instances in which the bullae were large and widespread and the whole onset seemed most severe, but in which spontaneous complete recovery resulted in from forty-eight to seventy-two hours. I doubt that this could have been possible in so many cases if otitis media were uniformly present. The character and brief course of the pain in many cases are unlike those noted in otitis media with comparably severe onset.

Furthermore, the occurrence of bullae on the wall of the canal without involvement of the tympanic membrane is also contrary to the conception that otitis media was uniformly present.

Finally, if otitis media were uniformly present prior to the appearance of the bullous lesions, it is striking how relatively infrequently this otitis media presented its characteristic signs and symptoms or how relatively infrequently frank otitis media was complicated by myringitis bullosa haemorrhagica.

Except for the possibility of the existence of a mild, perhaps subclinical, otitis media, which is not recognizable in the ordinary examination, the impression gained is that the bullous hemorrhagic myringitis is in most instances just what the name implies, external otitis.

CONCLUSIONS

I believe that although the series of observations is rather small, it indicates a definite trend and therefore justifies the following conclusions:

1. Myringitis bullosa haemorrhagica is a common complication of all infections of the upper respiratory tract and of the contagious diseases in the children of New York.

2. Although the picture presented by these patients resembles that described as influenzal otitis, the data indicate that the condition described here is a milder disease than that seen with influenza.

3. In 90 per cent of the involved ears the condition resolved spontaneously, thus justifying the conservative treatment of this condition.

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Case Reports

BACTERIAL (MYCOTIC) ANEURYSM OF THE POSTERIOR TIBIAL ARTERY

A CASE IN AN EIGHT YEAR OLD CHILD IN WHOM VASCULAR CHANGES PRECEDED RUPTURE OF THE LEFT CEREBRAL ARTERY

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The many articles written in the past century concerning aneurysm contain only a few reports of infectious (myotic) aneurysm of intravascular origin in patients under 10 years of age. An aneurysm may be congenital, traumatic, syphilitic, infectious or atheromatous in origin. Stengel and Wolferth [1] have thoroughly reviewed the subject of aneurysm of bacterial origin. It seems to me that the term bacterial or infectious aneurysm should replace the term mycotic aneurysm, as suggested by Osler [2] and Eppinger.[3] The wall of an artery or vein may become infected from without (periarteritis) or from within (endarteritis), with the formation of an aneurysm as a secondary result. The most common cause of periarteritis is the extension of infection to the wall of a vessel from a nearby inflammatory focus. Tuberculosis is one of the etiologic agents.

A less common type of periarteritis is known as periarteritis nodosum (Kussmaul's disease). Dickson [4] prefers the term polyarteritis nodosa because of the number of vessels usually affected. The bacterial cause of periarteritis nodosum is, in general, the streptococcus, which invades the tissues by way of the periarterial lymphatics.

In this report I am interested in aneurysm resulting from endarteritis rather than from periarteritis. It is due to lodgment of septic emboli in an artery or in the vasa vasorum as a result of a septic thrombus or the vegetation of acute endocarditis. Virchow, in 1847,[5] was probably

1. Stengel, A., and Wolferth, C. C.: Mycotic Bacterial Aneurysms of Intravascular Origin, Arch. Int. Med. **31**:527 (April) 1923.

2. Osler, W.: Brit. M. J. **1**:467, 1885.

3. Eppinger, H.: Arch. f. klin. Chir. (supp.) **35**:1, 1887; cited by Stengel and Wolferth.[1]

4. Dickson, C., in Boyd, William: The Pathology of Internal Diseases, Philadelphia, Lea & Febiger, 1931.

5. Virchow, R.: Virchows Arch. f. path. Anat. **1**:272, 1847.

the first person to write about the destructive changes in the wall of the vessel at the site of the embolus. Other men at that time thought the aneurysm was produced solely by pressure from behind the embolus. Goodhart [6] advanced the theory that infection plays a part in the formation of the so-called embolic aneurysm. After his publication, several investigators reported cases in which infection had been found in the wall of an aneurysm of malignant endocarditis. In 1887 Eppinger [3] described the minute changes that take place in the formation of "mycotic embolic aneurysm." In his opinion the infecting organism is carried to the adventitia and the infectious process later spreads to the media and intima.

According to Maximow and Bloom,[7] the walls of all arteries and veins with a caliber greater than 1 mm. are provided with their own blood vessels, the vasa vasorum. They form a dense capillary network in the adventitia.

In most cases, an infectious aneurysm is probably produced by lodgment of the infectious organism in the vasa vasorum of the adventitia, where the chief changes of acute arteritis are found. The entire thickness of the wall becomes infiltrated later by the products of inflammation, with weakening of the vessel wall which may result either in the formation of an aneurysm or in rupture of the vessel. The infectious organism is usually Streptococcus viridans, although in a few cases the influenza bacillus, the meningococcus, the staphylococcus or the gonococcus has been found. Healed rheumatic endocarditis or a congenital cardiac lesion usually predisposes to bacterial endocarditis, which in turn occasionally results in an aneurysm. Bacterial endocarditis occurs most commonly between the ages of 15 and 30 years. Endocarditis due to Str. viridans in children under 10 years of age is relatively uncommon. Leech [8] reported sixteen cases, in nine of which the patient was under 10 years of age, while Blumer [9] cited three hundred and seventeen cases in only one of which the patient was in that age period. In only 1.7 per cent of the cases of Lawson and Palmer [10] was the patient under 10 years; however, these authors stated that the lack of evidence in the early records for the diagnosis of subacute bacterial endocarditis makes this figure doubtful. Rost and Fisher [11] reported

6. Goodhart, J. F.: Tr. Path. Soc. London **28**:107, 1877.

7. Maximow, A. A., and Bloom, William: Text-Book of Histology, ed. 2, Philadelphia, W. B. Saunders Company, 1934.

8. Leech, C. B.: Am. J. M. Sc. **180**:621, 1930.

9. Blumer, G.: Medicine **2**:105, 1923.

10. Lawson, G. M., and Palmer, R. S.: New England J. Med. **199**:1205, 1928.

11. Rost, W. L., and Fisher, A. E.: Subacute Bacterial Endocarditis in Childhood, Am. J. Dis. Child. **36**:1144 (Dec.) 1928.

twelve cases, in four of which the patient showed some cerebral embolic phenomena, while in four of the sixteen cases reported by Leech [8] the patient showed some evidence of embolism.

The inflammatory process of acute rheumatic fever usually heals by fibrosis, but arterial lesions sometimes develop so rapidly that repair is impossible, and an aneurysm, with or without rupture, results.

I was able to find only two cases of aneurysm of the intracranial vessels in children under 10 years old.

REPORT OF CASE

G. P., a white boy 8 years of age, was admitted to the Presbyterian Hospital, Chicago, Oct. 29, 1935, with complaints, as given by the mother, as follows: "pain in the left kneecap—can't put left leg down," twelve days' duration; "fever from 100 to 102 F., with night sweats," two months' duration.

Present Illness.—The patient was apparently well until two months before admittance, when his left great toe became swollen and extremely painful. Within the next four days the other toes of the left foot became involved. The left ankle and elbow were then affected. The swelling and tenderness of each joint lasted about two days. After symptoms in the joints, he had severe pain in the left upper quadrant of the abdomen, which lasted four days. During the two months before his admission pain and swelling returned in the left foot and ankle on several occasions. Twelve days prior to his admission the left kneecap became swollen and tender, as a result of which he kept the leg in extreme flexion. He had severe pain in the leg when attempts were made to extend it. For the two months prior to admission he had a cutaneous eruption over the abdomen, chest and legs, which lasted for about two days and recurred on several occasions. The lesions were described by the mother as looking like mosquito bites.

History.—The patient had measles and diphtheria at 1½ years of age and rheumatic fever at 6 years.

Examination.—At examination the child was rather pale and was lying quietly in bed with the left leg in extreme flexion. There was a maculopapular eruption on the face, chest and left leg, which was regarded as toxic dermatitis. The conjunctivae were pale, and no petechiae were seen; the pupils were equal in size and shape and reacted to light and in accommodation. Examination of the mouth revealed five carious teeth and a slight enanthem on the soft palate. The tonsils were large and cryptic and appeared to be infected.

The apical impulse was about 2 cm. to the left of the midclavicular line in the fifth intercostal space and was described as diffuse and forceful. There was a palpable systolic thrill at the apex. The cardiac sounds were indistinct. There were presystolic and systolic murmurs in the mitral area, which were transmitted to the back and axilla, as well as systolic and diastolic murmurs in the aortic and pulmonic areas.

The lungs were normal. The spleen and liver were palpated 1.5 and 4 cm., respectively, below the costal margin. There was no tenderness. The left leg was in extreme flexion and was painful on manipulation. The proximal one third of the calf muscles was tender and of a doughy consistency. Pulsation was absent over this area and in the posterior tibial artery and was diminished in the dorsalis pedis artery. There were water hammer pulse and capillary pulsations.

Laboratory Findings.—Examination of the blood showed: hemoglobin (Newcomer) 73 per cent, red cells 5,270,000, white cells 18,200, neutrophils 74 per cent, small monocytes 19 per cent, large monocytes 6 per cent and eosinophils 1 per cent. On October 31 Wassermann and von Pirquet tests were made, the results being negative. A culture of the blood showed Str. viridans. On November 8 the rate of sedimentation of the erythrocytes was observed, microscopically, to be 35 mm. an hour.

Course.—On October 30 the left leg was extended without much difficulty. Soon after severe pain developed in the proximal third of the calf muscles.

On November 14 the mass gradually became larger and tenser. A slight pulsation and systolic bruit had developed.

On November 17 the child complained of pains in his leg and head. He became restless and delirious and vomited several times during the night.

On November 18 hemiplegia gradually developed on the right side, with convulsion-like seizures on the left. The patient gradually became comatose. During his period in the hospital his temperature had varied between 100 and 104 F. and his pulse rate between 120 and 160 per minute.

Death occurred at 11: 48 p. m. on November 19.

Autopsy (Dr. Carl W. Apfelbach).—The anatomic diagnoses were: subacute thrombo-ulcerative aortic, mitral and tricuspid endocarditis (Str. viridans); chronic indurative aortic, mitral and tricuspid endocarditis; mycotic aneurysm of the left posterior tibial artery; extensive hemorrhage into the muscles of the left calf; mycotic aneurysm of a branch of the left middle cerebral artery; spontaneous cerebral hemorrhage on the left side; anemic infarcts of the kidneys and spleen; petechial hemorrhage of the palpebral conjunctiva of the right eye; hyperplasia of the spleen; anemia; emaciation; marked cloudy swelling of the liver; bronchial aspiration of the contents of the stomach; hypertrophy of the wall of the left ventricle; fibrous pleuritis on the left side, and chronic passive hyperemia of the lungs.

The body was that of a white boy weighing 47 pounds (21.3 Gm.) and 124 cm. long. There were three petechial hemorrhages in the palpebral conjunctiva of the right eye. The skin of the entire body showed pallor. There were extensive swelling and purple discoloration of the left calf, especially in the posterior surface. Approximately 10 cm. inferior to the knee joint, the soft tissues were fluctuant.

The posterior tibial artery on the left side was incised from the knee joint inferiorly. It led into a hemorrhage about as large as a clenched fist, in the muscles of the calf. The wall of the artery ended abruptly in the hemorrhage. The inferior, torn margin of the artery was slightly swollen. For a distance of 5 cm. the remnants of the wall could not be identified. Beyond this point the artery was again seen. There was no gross alteration in the wall below the region of hemorrhage.

After the calvarium was removed, the dura was found to be uniformly tense throughout. The convolutions were flattened. On the left side, along the rolandic fissure, there was brown pigment, and the brain underneath the meninges was discolored a pale yellow-brown. The region of maximum change was 5 cm. in its maximum diameter, extending from about 1.5 cm. from the superior longitudinal sinus laterally along the rolandic fissure.

After hardening in a solution of formaldehyde the brain was cut into coronal sections. There was a hemorrhage in the left cerebral hemisphere, beginning at the level of the optic chiasma and extending posteriorly to the posterior horn of the left lateral ventricle and from the midline to within 1 cm. of the lateral surface of the hemisphere. All portions of the hemorrhage were homogeneous except in the anterior portion, near the lateral margin of the hemisphere, where there was a

circular region about 18 mm. in diameter, in which there were thin concentric rings. Grossly, this appeared to be the remnant of a dilated blood vessel.

The heart weighed 240 Gm. The aortic cusps were altered by chronic changes which produced rounded, free margins. The cusps no longer covered the sinuses of Valsalva when flattened against their walls. The maximum change was in the posterior cusp. In the ventricular surface of the left cusp, 3 to 4 mm. from the nodulus Arantii, there was a light gray-pink mass 2 to 3 mm. in diameter. The maximum deposit of this material was on the left aortic cusp. It extended inferiorly onto the base of the anterior mitral leaflet. The wall of the left ventricle was firm. On the ventricular septum there were a few rounded, interlacing, opaque elevations of the endocardium immediately inferior to the left cusp. The mitral leaflets were shortened and thickened. The chordae tendineae were short and thick. Between them most of the normal, thin membrane of the leaflet had disappeared. There was a small ulceration of the posterior leaflet at its middle that extended to within 3 mm. of the base of the leaflet. The lining of the left auricle was gray and opaque, whereas that of the right was translucent and much thinner. The mitral ring was 6.8 cm. in circumference, whereas the aortic ring was 5 cm. The pulmonary cusps were normally formed. The tricuspid ring was 9.5 cm. in circumference. In the medial tricuspid leaflet, the free margin was ulcerated and discolored by hemolyzed blood.

The spleen weighed 128 Gm.

Histologic Examination: In a section through the proximal end of the left posterior tibial artery, close to where it entered the hemorrhage in the left calf, there was a subacute inflammatory change in the subintimal layer. There were a considerable number of polymorphonuclear leukocytes and recently proliferated fibroblasts. In the adventitia and surrounding tissues, there were hemorrhage and an extensive exudate of polymorphonuclear leukocytes. In other sections through the hemorrhage, fragments of muscle, walls of veins and polymorphonuclear infiltrations in fibrous tissue were observed, but no other portions of arterial wall.

In a section of the left cerebral hemisphere near the rolandic fissure, there were necrosis and an abundance of phagocytic cells, indicating infarction or hemorrhage previous to the recent large hemorrhage. In sections through the circular region resembling a dilated blood vessel, fragments of fibrous tissue and hemorrhage were observed, and polymorphonuclear cells were the only cells identified.

No change was found in the cerebral artery or in the right posterior tibial artery to indicate the presence of an aneurysm. The inflammatory change in the wall of the left posterior tibial artery, together with the proliferation of fibroblasts, suggests that an embolic lesion was present in the wall of the artery several days or a few weeks before death. In the case of the left cerebral artery, no changes were identified to prove histologically that the primary lesion in the wall of the artery was a mycotic lesion. However, before the extensive hemorrhage occurred in the brain, there had been localized vascular disturbance, as demonstrated by the numerous phagocytic cells, hemosiderin pigmentation and necrosis.

CASES REPORTED IN THE LITERATURE

CASE 1 (*Moutard-Martin* [12]).—A boy 2 years of age had subacute endocarditis, congenital heart disease and an aneurysm of the ascending portion of the aorta. No autopsy was performed.

12. Moutard-Martin: Bull. Soc. anat. de Paris **10**:775, 1875; cited by Richey, W. D.: Intrapericardial Rupture of Aortic Aneurysm in a Boy Sixteen Years of Age, Arch. Int. Med. **31**:232 (Feb.) 1923.

CASE 2 (*Moore*[13]).—A girl 5 years of age had a history of rheumatism. She had been ill for six weeks. A double murmur was heard at the base and a systolic murmur at the apex of the heart. There was clubbing of the fingers and toes. Death was due to embolism.

Autopsy revealed an aneurysm of the right common iliac artery. The heart was hypertrophied, and there were vegetations on the aortic and mitral valves.

CASE 3 (*Withe,*[14] *reported by Jacobi*).—A girl 7 years of age in whom rheumatism had developed when she was 3 years of age, had a well marked valvular lesion. An aneurysm of the left femoral artery appeared first and was followed by a tumor in the right inguinal region. Death was due to malignant ulcerative endocarditis.

Autopsy revealed an aneurysm of the right external iliac artery, femoral arteritis, vegetations on the mitral valves and thickening of the aortic valves.

CASE 4 (*Voolker*[15]).—A girl 1½ years of age had aortic valvular disease. Death was due to capillary bronchitis.

Autopsy revealed an aneurysm and some endocarditis of the aortic valve. There was no other valvular disease.

CASE 5 (*Alexejew*[16]).—A girl 10 years of age had pain and depression for eight weeks. There were palpable pulsations under the umbilicus. The pulse in the left crural artery was smaller than that in the right.

Autopsy revealed an aneurysm of the abdominal aorta and vegetations on the mital valve.

CASE 6 (*Aitken*[17]).—A boy 9 years of age had a history of several rheumatic attacks and pain in the chest. There were no circulatory disturbances. The diagnosis was aneurysm of the abdominal aorta. Death was due to embolism.

CASE 7 (*Gabriel*[18]).—In a boy 10 years of age with endocarditis, embolic hemoplegia and a hard, smooth tumor in the abdomen developed simultaneously.

Autopsy revealed ulcerative endocarditis, cerebral emboli and an aneurysm of the superior mesenteric artery.

CASE 8 (*Le Boutillier*[19]).—A girl 9 years of age had a history of rheumatic fever. The superficial veins of the chest, face, neck and arms were engorged. Pulsation was present over the cardiac region, the suprasternal notch and the vessels of the neck. There was tracheal tug. The radial pulse was weak. The pulse on the left side was weaker and slower than that on the right. A loud harsh murmur was heard over the dull area and less distinctly throughout the thorax. A systolic and a presystolic mitral murmur were present. The diagnosis was aneurysm of the ascending part of the aorta.

CASE 9 (*Jordan*[20]).—A boy 6 years of age had septic aortitis, with embolism of the vasa vasorum, and an aneurysm of the ascending part of the aorta, with intrapericardial rupture.

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13. Moore, N.: Tr. Path. Soc. London **34**:71, 1882.

14. Withe, G. M., reported by A. Jacobi, taken from Le Boutillier, T.: Am. J. M. Sc. **125**:778, 1903.

15. Voolker, A. F.: Tr. Path. Soc. London **45**:51, 1893.

16. Alexejew, N. N., cited by Le Boutillier, T.: Am. J. M. Sc. **125**:778, 1903.

17. Aitken, R. Y.: Brit. M. J. **1**:1655, 1898.

18. Gabriel, cited by Lindborn, O.: Mitt. a. d. Grenzgeb. d. Med. u. Chir. **27**:912, 1914.

19. LeBoutillier, T.: Am. J. M. Sc. **125**:778, 1903.

20. Jordan, A. C.: Lancet **1**:515, 1903.

CASE 10 (*Klotz* [21]).—A boy 6½ years of age had a history of rheumatic fever six months before admission to the hospital. On admission he had active rheumatic fever, with pains in the joints, intermittent fever, choreiform attacks and restlessness. He died four days after admission. The diagnosis was aneurysm of the ascending portion of the aorta. A blood culture showed short chain streptococci.

CASE 11 (*Fahr* [22]).—A girl 6 years of age had no history of rheumatic fever. She had fulminating staphylococcic pyemia from ulcerative endocarditis of the tricuspid valve. Staphylococcic metastasis extended to almost all the organs. A blood culture showed Staphylococcus aureus. Death was due to a ruptured aneurysm of a branch of the left middle cerebral artery.

CASE 12 (*Baginsky* [23]).—A boy 7¾ years of age had no history of rheumatic fever, but he had pain in the extremities on admission. There were embolic phenomena of the right radius and a pulsating mass in the midabdomen, and a bruit was heard. Autopsy revealed a large aneurysm of the abdominal aorta and a small aneurysm of the right subclavian artery.

CASE 13 (*Calvin* [24]).—A girl 9 years of age had a history of five attacks of chorea. The onset of the first attack was five years previous to her admission to the hospital. The diagnosis was thoracic aortic aneurysm with chronic endocarditis and hypertrophy of the heart.

CASE 14 (*Lawson and Palmer* [10]).—A girl 10 years of age had no history of rheumatic fever. She had a fever caused by sepsis. A blood culture was negative. Autopsy showed that the bicuspid aortic valve had cauliflower-like vegetations and two mycotic aneurysms, one of the valve cusp and one in the first portion of the aorta. There was rheumatic endocarditis of the mitral valve.

CASE 15 (*Forbus* [25]).—The patient was 8 years of age. The sex was not stated. The diagnoses were endocarditis due to Str. viridans, multiple abscesses of the brain, a ruptured mycotic aneurysm of the basilar artery and meningitis.

CASE 16. (*Craig* [26]).—A boy 10 years of age had had "heart disease" since he was 3 years of age. There was no history of rheumatic fever. He had hemiplegia, followed by chills and pains in the joints and muscles. Forty-eight days later a tumor of the left femoral artery was noted. Seven blood cultures were negative. The eighth blood culture showed B. influenzae.

CASE 17 (*Wolffe* [27]).—A girl 7 years of age was seen in 1922. She had a history of rheumatism, rheumatic heart disease and an aneurysm of the arch of the aorta. She was still living in 1932.

In the seventeen reported cases I was able to find two cases of aneurysm of the intracranial vessels. In three cases the patient had double aneurysm. In ten cases the aneurysm was aortic; in three it was located in the abdominal portion, whereas in five it was definitely

21. Klotz, O.: J. Path. & Bact. **18**:259, 1913.

22. Fahr: München. med. Wchnschr. **53**:96, 1906.

23. Baginsky, A.: Berl. klin. Wchnschr. **1**:144, 1908.

24. Calvin, J. K.: Aneurysms of the Thoracic Aorta in Children, Am. J. Dis. Child. **21**:327 (April) 1921.

25. Forbus, W. D.: Bull. Johns Hopkins Hosp. **47**:239, 1930.

26. Craig, J. D.: Femoral Aneurysm During Subacute Bacterial Endocarditis in Childhood, J. A. M. A. **97**:245 (July 25) 1931.

27. Wolffe, J. B.: Arch. Pediat. **49**:100, 1932.

in the ascending portion. The femoral artery and the cusps of the aortic valve were each involved in two cases. The common iliac, external iliac, subclavian and superior mesenteric arteries were each affected in one case.

As to sex, there were nine girls and seven boys, and in one case the sex was not mentioned.

The age of the patients was as follows: 10 years, four; 9 years, three; 8 years, two; 7 years, two; 6 years, three, and 5, 2 and 1½ years, one each.

SUMMARY

A case of septic aneurysm of the posterior tibial and of the left cerebral artery is reported. The literature is reviewed.

ACUTE LUPUS ERYTHEMATOSUS DISSEMINATUS

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Acute lupus erythematosus disseminatus is not a common disease in childhood, and there is little reference to it in American pediatric literature.[1] Recent writers, dermatologists and internists, have approached the condition as a manifestation of systemic disease. Indeed, this particular cutaneous lesion seems now to be just emerging from the same sort of confusion that surrounded the erythema group of diseases when Osler described them. It is in relation to the concept of lupus erythematosus disseminatus as a manifestation of systemic disease that we record this case.

REPORT OF A CASE

A 7 year old Jewish girl was admitted to the pediatric service of the Mount Sinai Hospital on Aug. 20, 1935. The family history was of interest in that the mother, who was 40 years of age, had been treated seventeen years previously for a lesion on the nose, which had been diagnosed as lupus erythematosus of the discoid type. There was no history of tuberculosis in the family. The child had had whooping cough, chickenpox and measles, and a tonsillectomy had been done three years previously. She had had vaccination for smallpox and immunization for diphtheria. Six weeks before her admission to the hospital, after she had spent a day at the beach, moderately severe sunburn of the face, shoulders and arms developed. This subsided after a few days, and one week later (five weeks before admission) the child was again exposed to the sun and a more severe burn developed over the same area. This healed apparently without blistering or desquamation. The skin was then clear until about the last week in July (four weeks before admission), at which time a red papular eruption appeared on the nose and spread over both cheeks in a typical butterfly arrangement. This did not itch or burn, but it gradually became more intensely red and more extensive, going down to the shoulders and the upper portion of the chest. For the past three years the child had complained occasionally of transient pains in the joints. One week before admission she again complained of pains in the

From the pediatric service (Dr. Béla Schick, director) and the laboratories of the Mount Sinai Hospital.

1. Lyon, J. M.: Acute Lupus Erythematosus, Am. J. Dis. Child. **45**:572 (March) 1933. Cummer, C. L.: Lupus Erythematosus in Infancy and in Childhood, Arch. Dermat. & Syph. **24**:999 (Dec.) 1931. (Refers to many cases in children, but no distinction has been made between acute lupus erythematosus disseminatus and the discoid form.) Gawalovski, K.: Acta dermat.-venereol. **10**: 1, 1929. (Presents an excellent review and discussion of the various theories of the etiology.)

fingers, knees and ankles; the pains were transient and were never associated with redness or swelling. It was at about this time that the parents first noted a daily elevation of the temperature to 100 or 101 F. The child's appetite had become progressively worse, and her general condition did not seem as good. Because of the eruption she was seen by a physician, who advised hospitalization.

On admission the child appeared well developed and well nourished. The temperature was 100 F. She complained of pain in both hands on the dorsal surface at the base of the thumb. On examination, a reddish violet, diffuse, slightly elevated, confluent eruption was noted covering the nose, both cheeks and the forehead. This had a typical sharply defined edge. The lesion was studded with dark brown pigmented areas, and slight scaling was noted. There

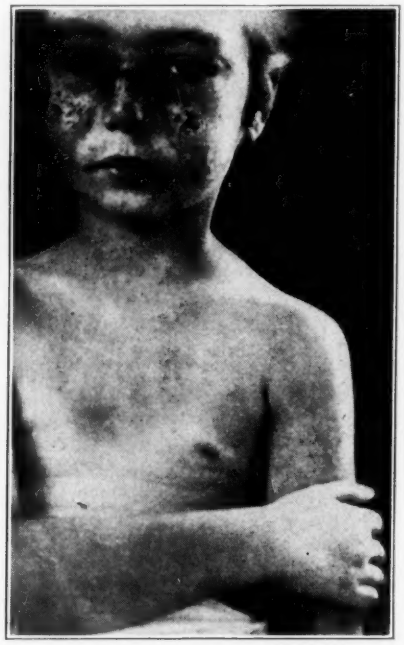

Fig. 1.—Lesions of the face and neck, conforming to the neck line of a bathing suit. The lesions of the arm are less obvious.

was no crusting or vesiculation. Pinkish, slightly elevated areas from 3 to 5 mm. in diameter were noted over the arms to about 2 inches (5 cm.) above the wrists. In addition, a few scattered lesions were present on the anterior surface of the upper part of the chest. These were circumscribed and conformed to the neckline of a bathing suit. Both external ears were red, slightly swollen and tender. The spleen was palpable about 1 cm. below the costal margin in the anterior axillary line; it was hard but not tender. Examination of the heart gave negative results. The lungs were normal. At the angle of the mouth on the right, a red, ulcerated area was noted. The buccal mucosa and the inner surface of the lips were studded with many red, elevated lesions measuring about 2 mm. in diameter. An exceedingly thick, mucopurulent postnasal drip was noted. The fundi were normal.

Roentgen ray examination of the chest showed no abnormality, and examination of the paranasal sinuses failed to show any evidence of disease. The electrocardiogram was essentially normal on admission, and subsequent examinations showed no appreciable change. Close observation of the heart during the entire period of hospitalization failed to show any signs of pathologic change. The blood pressure was consistently high, ranging between 104 and 122 systolic and between 70 and 90 diastolic.

During the first three weeks of observation the question frequently arose as to the advisability of removing an evident and easily accessible focus of infection, namely, some abscessed teeth. The danger of causing exacerbation, with infection of the blood stream, was carefully weighed against the advantages of such a procedure. It was finally decided to extract one of the abscessed teeth. When the child became afebrile and her general condition appeared satisfactory, this was done. A blood culture taken immediately after this procedure was negative. The following day the child's temperature became elevated to 102 F., and her general condition appeared decidedly worse. It was then felt that any further attempt at removal of questionable foci of infection was contraindicated.

During the subsequent few months the child's general condition seemed to remain about the same. Urinalysis persistently showed a 2 to 3 plus reaction for albumin, from 0.25 to 0.5 Gm. per thousand cubic centimeters in twenty-four hours by the Esbach test. The specific gravity ranged between 1.014 and 1.022. There were 10 white cells and 3 or 4 red cells per high power field, in addition to cellular and granular casts. Kidney concentration tests were within normal limits.

On admission, a blood count showed hemoglobin 70 per cent, red cells 5,100,000, white cells 10,000 and polymorphonuclears 69 per cent. Progressive anemia and leukopenia slowly developed. The hemoglobin content dropped to 50 per cent and the white cells to 4,900. Leukopenia was constant thereafter.

Cultures of material from the nose and throat showed the presence of Streptococcus haemolyticus, Staphylococcus aureus, Staphylococcus albus and diphtheroid bacilli.

Chemical examination of the blood revealed figures within the normal range, as follows: sugar 95 mm., chlorides 585 mg., urea 11 mg., total protein 6.1 Gm., albumin 3.4 Gm., globulin 2.7 Gm., cholesterol 200 mg. and fibrinogen 410 mg., per hundred cubic centimeters. Both the galactose tolerance test and the congo red test were normal. The Takata-Ara test was positive. This may be considered a possible indication of some damage to the liver. Schick, Wassermann and tuberculin tests were negative.

Five months after admission severe otitis media developed, with a temperature of 103 F. Myringotomy was performed. The temperature showed daily elevations to 104 F. for a period of one week, and then it dropped by lysis for an additional week. A roentgenogram of the chest showed a small pneumonic infiltration in the lower lobe of the right lung. A culture of pus from the ear contained type IV pneumococci. A culture of material from the throat at this time also showed type IV pneumococci in addition to Streptococcus viridans, Staph. aureus and Staph. albus. A blood culture was negative. The child was given a transfusion of 250 cc. of citrated blood.

A month later, six months after admission, tenderness developed in an inguinal lymph node on the right side. The following day the temperature rose to 105 F. and the child's general condition seemed worse. A blood culture at that time was negative. Thereafter until death, four days later, the temperature ranged between 103.5 and 106.8 F. The day before death the patient complained of pain in the right posterior axillary region, which was aggravated by deep

inspiration. Resonance in this area was not impaired, but a transient friction rub could be heard. Râles were present over both bases; there were no bronchial breath sounds. That evening generalized convulsions occurred. Spinal puncture was done, and the fluid was clear. Colloidal gold, Wassermann and globulin tests were negative. The child went downhill rapidly and died with signs of pneumonia.

INVESTIGATIONS

During the course of the disease certain special tests were done. Some were suggested by the various theories concerning the etiology and pathogenesis of the condition and others by the daily bedside observation of the child. Even though most of the results proved to be negative, it seems advisable to record them. Lupus erythematosus disseminatus comprises such a heterogeneous group of conditions that negative results in one case do not necessarily imply that similar tests in other cases will also be negative.

The picture presented by capillary microscopy varied with the site observed and the stage of the disease. We shall record what seems to us to have been the

Fig. 2.—Hemorrhages beneath the fingernails.

evolution of the lesions. When the child was first admitted, the nail bed showed primarily two things, dilatation of the capillaries and slowing of the stream. Some areas showed more advanced lesions, stagnation of the corpuscles in rouleaux formation, without any movement of the stream, or a pendulum movement. The latter could be demonstrated more clearly by the application of a sphygmomanometer cuff. With pressure applied in the cuff, one saw the capillary lumen and within it and separated by a clear zone of serum a strand of yellow agglutinated corpuscles that looked like a string of misshapen gold pieces. Where frank hemorrhage occurred, only an amorphous mass of discolored substance and no capillaries could be seen. Later, when the skin of the finger tips looked atrophied and some of the extravasated blood had been absorbed and part of the nail bed looked white, we observed in some places a different capillary reaction. The capillaries could be seen as only thin, straight red lines. We interpreted this as shrinkage, fibrosis or scarring of the capillaries after prolonged stagnation of the red cells within them.

Are these lesions characteristic or pathognomonic? Our own experience in capillary microscopy is too limited to permit an independent opinion. Dr. Sidney Leader made these observations of the capillaries of the skin with us, and the following comments are the result of

conference and discussion with him. Similar observations have been made in one other instance, a case of dermatomyositis with cutaneous lesions similar to those of lupus erythematosus disseminatus. The relationship of this condition to lupus erythematosus disseminatus is being studied.[2] The descriptions of the capillaries in "lupus erythematodes" in Müller's atlas[3] do not correspond with ours, nor, in fact, have we found in any other paper a reference to capillary pictures identical with ours. It is difficult, however, from the pictures or descriptions of others to be sure that lesions similar to those in our case have not been found in other conditions. What seems most characteristic of the capillary picture in lupus erythematosus disseminatus is not so much the appearance of the capillary bed at any single observation as the sequence of events, the change in the capillaries with the evolution of the disease. We are not prepared to say that even this is pathognomonic, but we suggest that the evolution of the lesions just described is at least characteristic of the disease.

The patient's reaction to the removal of a tooth suggested that during a prolonged period of illness a patient may acquire an unusual degree of sensitivity even to his own proteins or metabolic products. Cutaneous tests were done with the child's own serum, with extracts of human placenta supplied by Dr. Karelitz and with horse serum. The results were all negative.

One theory of the cause of lupus erythematosus disseminatus is that it is the result of a streptococcus toxin. Because of this possibility, Dick tests were performed. It was necessary to raise the dose to 120 units before a positive reaction was obtained. We do not know how to evalute this finding. Dr. Dick has advised us that it is unusual, that there are few people who fail to give a cutaneous reaction with such large doses of toxin.[4]

An effort to find toxin in the blood was made by the passive transfer (Prausnitz-Küstner) method. Photosensitivity of the skin might have been due to some substance which, circulating in the blood, sensitized the skin to sunlight. Therefore, some of the patient's serum was injected intracutaneously into one of us. After the usual interval the areas of injection, as well as untreated skin, were exposed to a strong erythema dose of ultraviolet radiation. No lesions resembling those of lupus erythematosus disseminatus appeared. A "sunburn" erythema occurred, which was similar or identical in intensity on the treated and on the untreated areas of the skin.

The possibility that the capillaries might show an unusual predisposition to damage led to a test of this hypothesis. Light stroking and heavy stroking with a fine and with a coarse implement of parts of the skin other than the sites of lesions elicited normal responses. Similarly, a needle prick through a drop of

2. Karelitz and Welt[13] called attention to the association of dermatomyositis and lupus erythematosus disseminatus. These two and other allied conditions will be the subject of a further study by Karelitz, Welt, Bass and Denzer.

3. Leader, S. D.: Capillary Microscopy in Children, Am. J. Dis. Child. **44**: 403 (Aug.) 1932. Müller, O.: Die Kapillären der menschlichen Körperoberfläsche in Gesunden und Kranken, Stuttgart, Ferdinand Enke, 1922.

4. Dick: Personal communication to the authors.

solution of epinephrine hydrochloride (1 to 1,000) demonstrated contraction of the capillaries. The moccasin snake venom test for permeability of the capillaries, developed by Peck and Rosenthal,[5] also showed a normal reaction. Thus no evidence could be adduced of abnormal predisposition of the capillaries to damage.

The presence of circulating toxin was sought by means of the Shwartzman phenomenon.[6] A positive reaction was twice obtained with the patient's serum and blood. That is, when a toxic filtrate of typhoid bacilli was used as a preparatory dose, the subsequent intravenous injection of the patient's serum or blood produced a positive phenomenon. The reverse, the use of the patient's serum as a preparatory dose, was unsuccessful. Unfortunately, one cannot assume that this is evidence of a toxic factor. Such reactions may be found in patients with other

Fig. 3.—Lesions of the foot.

conditions and even when present may be evidence of a combination of antigen and antibodies. A similar search for a circulating toxin by Schifrin using the Shwartzman phenomenon gave negative results in several cases.[7]

The posterior tibial and the dorsalis pedis pulse were investigated. At first the absence of pulsation in both the anterior and the posterior vessels of the right foot seemed constant. Persistent observation showed that this was not the case. However, one could not regularly feel the pulsations in both feet; at

5. Peck, S.; Rosenthal, N., and Erf, L. A.: The Value of the Prognostic Venom Reaction in Thrombocytopenic Purpura, J. A. M. A. **106**:1783 (May 23) 1936.

6. These tests were performed in Dr. Shwartzman's laboratory.

7. Schifrin: Personal communication to the author.

times one pulse would be missing and at times another, and even when pulsation was present it was more difficult to observe than in other children of the same age. Quantitative oscillometric readings could not be made because of the absence of standards and a standard cuff for children of this age. Dr. Averbuch, who has had wide experience in peripheral vascular disease in adults, controlled our observations. Qualitative tests with the oscillometer and palpation by Dr. Averbuch confirmed our finding of frequent absence of pulsation and difficulty in palpation. The question arose as to the significance of these observations. Heretofore, in cases of this type the subject had shown at necropsy changes only in vessels of small caliber. It was conceivable, however, that larger vessels might also be involved. With that thought in mind, we removed a small piece of the dorsal vein of the leg after a transfusion.

The histologic examination was done by Dr. Paul Klemperer. He reported that the intima was thickened, being about twice as thick as the media, and that the adventitia was vascular and consisted of thick bundles of connective tissue. He was reluctant to pass judgment on the significance of these observations; the occasion for examining peripheral veins does not present itself often enough to supply a background for comparison with this one observation in a girl of 7 years. In general, the exposed position of these peripheral veins might subject them to enough trauma to explain the degree of endophlebitis found. Martin and Tull described a similar condition in a fairly large percentage of children examined as a routine who did not show any evidence of vascular disease. We are inclined to believe that the observation of phlebosclerosis in our case is of no special significance.

AUTOPSY REPORT

The significant part of the necropsy was the histologic examination. Hence, the gross pathologic changes are summarized briefly.

The autopsy was done within a few hours of death. The entire scalp was covered by a mass of yellow, oily, confluent crusts, and the cheeks and forehead showed purplish, macular patches and dots. The nostrils and mouth were fissured and covered with dry bloody crusts. The entire body was covered with coarse gray scales. The nail beds of the fingers and toes were thickened and spongy and showed clubbing. The peritoneal cavity contained a small amount of fluid and a few flakes of fibrin. The mesenteric glands were enlarged, and section showed a yellowish opaque zone beneath the capsule. The heart showed the following conditions: the myocardium of both ventricles was widened and enlarged, and the right ventricle had a small area of mural endocarditis. The valves were normal. The lymph nodes about the aorta and the external iliac arteries were enlarged. Both the right and the left lung showed areas of acute bronchopneumonia, and there were acute hemorrhagic fibrinous pleuritis on the right side and subpleural hemorrhages in the right lung. In the liver, the parenchyma projected above the cut surface, and there were white dotlike triangular areas interpreted as foci of necrosis. The spleen was large, adherent to the diaphragm and covered with stringy, reddish yellow material. The arteries were thickened. The capsule of the kidneys stripped easily; the cortex was widened and the corticomedullary junction indistinct; the cortical markings were blurred, and the medulla was somewhat congested. The pancreas, adrenals, genitals, gastrointestinal tract and bone marrow showed nothing significant. Lymph nodes in various parts of the body were enlarged—the interbronchial nodes and those about the hilus of the liver, within the lesser omentum and around the hilus of the

spleen and the renal pelves. The anatomic diagnoses were: acute disseminated lupus erythematosus; mural endocarditis of the right ventricle; acute pneumonitis, acute hemorrhagic fibrinous pleuritis and subpleural hemorrhages of the right lung; bronchopneumonia of the lower lobe of the left lung; edema of the liver, kidneys and heart; focal necrosis of the liver and lymph nodes; acute and chronic perisplenitis; acute fibrinous peritonitis, and hypertrophy of the left ventricle.

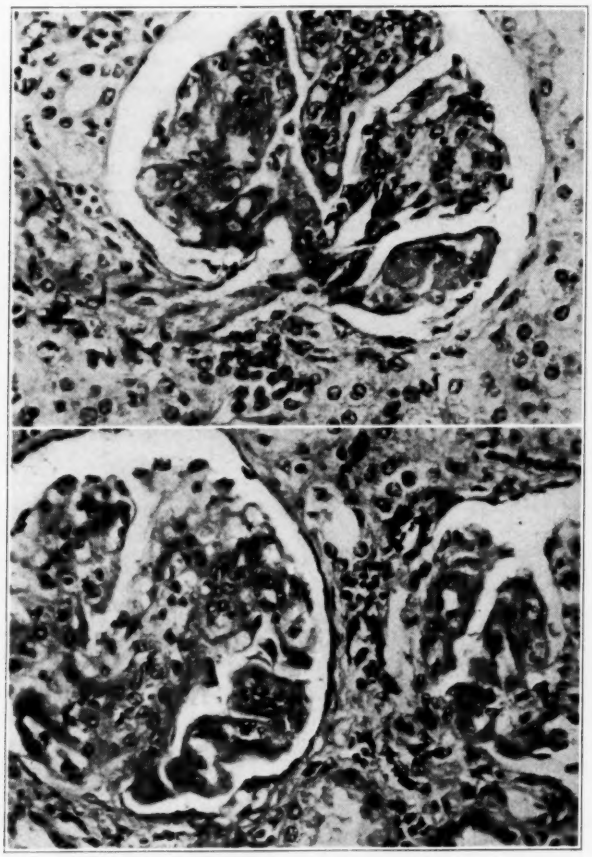

Fig. 4.—"Wire loop" lesions; hyaline thrombi.

Histologic examination gave the following results:[8]

The renal architecture was not altered. Right beneath the capsule and throughout the cortex a few foci of scarring were scattered, where the tubuli were atrophic and the stroma was increased, with slight infiltration by plasma cells and sporadic polymorphonuclear leukocytes and lymphocytes. In addition, there were foci where the tubuli were separated by the dilated meshes of the stroma, evidence of edema.

8. Dr. Paul Klemperer made the report of the histologic changes and provided the discussion of their significance.

The primary convoluted tubuli contained fibrillar and granular coagulated material and occasionally hyaline casts. A few tubuli contained red blood cells and others concentrically lamellated calcium particles. The lining epithelial cells were large and the cytoplasm coarse and granular; within some of the distal portions there were hyaline droplets. As a whole, the basal portions of the cells contained fat droplets only sporadically, but there were occasionally small groups of primary convoluted tubules where there was a conspicuous accumulation of doubly refractile neutral fat within the cells. The lumen of a few tubuli recti of the medulla was plugged with fatty casts.

The arterial ramifications were without changes except for the vasa afferentia, which will be described with the glomeruli. The intertubular capillaries were well filled but not engorged. The veins were not affected.

The glomeruli showed without exception characteristic changes, varying only in intensity. The most conspicuous alteration was homogeneous thickening of the capillary wall, which sometimes affected the entire tuft and sometimes only a few loops. The wall of the capillary stained homogeneous pink with eosin, red with Mallory's (azan) stain, yellowish brown with the Van Gieson-Weigert elastica stain and light brown with phosphotungstic acid and hematoxylin. The thickened capillary wall did not stain with sudan or with congo red (amyloid) or for fibrin. The conspicuous thickening of the wall, for which the term wire loop was appropriate, was due to the deposition of a substance between the layers of the basement membrane and the endothelial cells. This can well be demonstrated with azan stains. The visceral epithelial layer consisted of cells which were in part normal but in part showed degenerative cytoplasmic (hyaline droplet) changes and nuclear pyknosis. Many loops contained within their lumens hyaline globules, which gave the same reaction in staining as the hyaline deposits within the wall. The endothelial cells of the thickened loops showed pyknosis and occasionally elongated, bizarre nuclei. Where the lumen was filled, the endothelial cells broke up, and at a later stage apparently adjacent loops coalesced and parts of the glomerular tuft, occasionally the entire tuft, formed a homogeneous mass, with few remaining nuclei. Fusion of loops with the capsule was also frequent. In some loops the lumen was filled by the cytoplasm of endothelial cells which were vacuolated. On staining with sudan, such cells were observed to contain abundant neutral fat.

The vasa afferentia were patent, and occasionally a thickening of the intima was found, which was due to a deposit beneath the endothelium of a homogeneous substance similar to that of the glomerular capillaries. Bacterial stains gave negative results.

The lobular architecture of the liver was not disturbed. The cell cords were in regular, radial arrangement. The cells occasionally contained large fat vacuoles; otherwise there were neither cytoplasmic nor nuclear aberrations. The capillaries contained blood but were not unduly engorged. There was no pericapillary edema. In some areas of the section the stellate cells contained a large amount of iron pigment. The ramifications of the hepatic artery and of the portal and hepatic veins were without changes. The periportal fields were narrow and without cell infiltration or other irregularities.

The capsule of the spleen showed plaquelike thickening of the peritoneal coat, which presented a fibrous organization of a fibrinous exudate. The fibrin formed homogeneous trabeculae surrounded by fibroblasts. The subcapsular zone showed condensation of the cytoplasmic and fibrillar reticulum. The meshes were narrow. The reticulum meshes of the red pulp were engorged, and the

cords between the sinuses were rather cellular owing to the presence of plasma cells, lymphocytes, polymorphonuclear leukocytes and large basophilic mononuclear cells. Mobilized histiocytes were not conspicuous, and siderophages were encountered only occasionally. The smaller arteriolar branches were surrounded by a cellular mantle, consisting chiefly of plasma cells. The sheathed capillaries described by Schweigger and Seidel were easily recognized in the periphery of the splenic follicles. The venous sinuses were alternately engorged and less well filled with red cells; endothelial cells were not conspicuous. The white pulp was conspicuous because both the lymphatic sheaths and the follicles were well developed. The follicles showed only rarely small insignificant secondary follicles with degenerating epithelioid reticulum cells and disintegrated lymphocytes. The perifollicular zone was very cellular, and for this reason the malpighian follicle was not well defined from the adjacent red pulp. The most conspicuous feature, however, was perivascular fibrosis affecting most of the central and follicular arteries. The adventitia was surrounded by concentric interlacing lamellae of

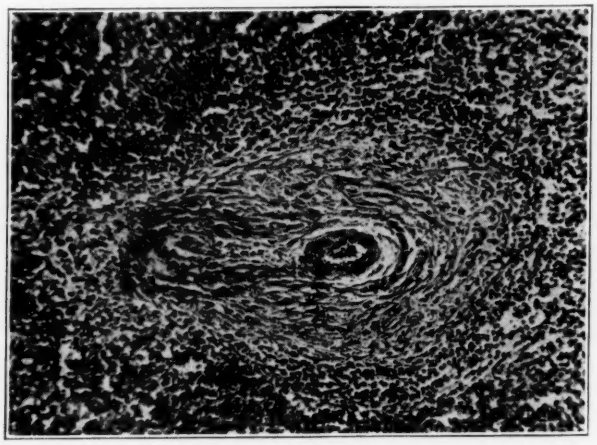

Fig. 5.—The spleen: perivascular fibrosis of the central artery.

connective tissue infiltrated by plasma cells and sporadic leukocytes. The thickness of these perivascular fibrotic rings was many times that of the diameter of the vessels. The vessel wall proper showed no changes.

There were no changes in the pancreas.

Cells of the adrenal cortex contained an abundant amount of lipoid. There were no changes. A small cortical adenoma, however, showed central necrosis. The periadrenal fat tissue was edematous.

The interbronchial and hilar nodes showed inflammation and perilymphadenitis. Strands of fibrosis were scattered throughout the lymphatic tissue of the peripancreatic nodes examined. A few small veins contained small thrombi (post mortem?). Another peripancreatic node showed, in addition, a large area of necrosis, surrounded by a reactive zone with many lipoid-containing histiocytes. The stain for tuberculosis gave negative results. A mesenteric lymph node showed acute lymphadenitis.

The bone marrow was very cellular and the ratio of bone marrow cells normal. No abnormal cells were present.

Sections of every part of the gastro-intestinal tract were examined, and the only changes noted were within the submucosa of the appendix, where a few arterioles, subintimal necrosis and circumscribed thrombosis were observed.

No changes were noted in the salpinx, ovary, uterus, vagina or bladder.

The middle and the lower lobe of the right lung showed extensive areas of bronchopneumonia with abscess formation. The pleura and the interlobular septums were infiltrated and also, secondarily, the walls of some large veins which showed parietal thrombi. In the upper lobe of the left lung there was no exudate within the alveolar lumens, but there was leukocytic infiltration of the interalveolar and larger septums. Many small vessels contained recent platelet thrombi.

The heart showed changes of the pericardium, myocardium and endocardium analogous to those observed by Gross and Friedberg in other cases of lupus erythematosus disseminatus, which they will report.

In a summary of the histologic changes, the renal lesions deserve most attention. The chief and most characteristic alterations were found within the glomeruli. They consisted of homogeneous thickening of the capillary wall identical with that described by Baehr, Klemperer and Schifrin [8a] in their report on lupus erythematosus disseminatus, termed wire loops. The thickening is due to a deposition of a homogeneous substance between the layers of the basement membrane. The nature of this substance cannot yet be determined by histologic methods, but lipoid, amyloid and fibrin can be ruled out because of the reaction to staining and the histologic appearance. The glomerular alteration does not resemble any phase of glomerulonephritis or glomerulitis often found in general infections. It is probably degenerative, because of the gradual destruction of the endothelial and epithelial cells with the final fusion of loops into a homogeneous mass. The presence of hyaline plugs within the capillary lumen enhances this final state of glomerular decay. Vascular lesions were not conspicuous except for occasional subendothelial deposits within the vasa afferentia, which seemed to be the result of an extension of the process within the glomerular capillaries into a proximal portion of the arterial tree. The degenerative lesions of the epithelium of the primary convoluted tubules as well as the early focal atrophy of the parenchyma can be regarded as secondary to the alteration of the circulation within the glomeruli. The lesions within the spleen consisted of striking perivascular fibrosis of the smaller arteries, a lesion which is quite unusual in itself but has been observed in several similar cases (Libman and Sacks,[9] case 2). Otherwise the spleen presented the histologic picture of inflammation commonly found in general infections. Several lymph nodes showed large foci of necrosis, a feature repeatedly observed in lupus erythematosus disseminatus. Histologically, the pneumonia was not unusual. The other organs did not show any changes of interest except the appendix, with vascular lesions. The absence of vascular lesions within the skin is difficult to understand in view of the striking alterations during life. Unfortunately, limitations in the authorization for necropsy prevented the removal of sufficient skin for study.

COMMENT

Among the interesting features of this case the following will be emphasized: (1) its occurrence in a female, (2) its insidious onset,

8a. Baehr, G.; Klemperer, P., and Schifrin, A.: A Diffuse Disease of the Peripheral Circulation Usually Associated with Lupus Erythematosus and Endocarditis, Tr. A. Am. Physicians **50**:139, 1935.

9. Libman, E., and Sacks, B.: A Hitherto Undescribed Form of Valvular and Mural Endocarditis, Arch. Int. Med. **33**:701 (June) 1924.

with arthralgia, a so-called rheumatic symptom, (3) appearance of cutaneous lesions after exposure to sunlight, (4) reaction to attempted removal of infected teeth, (5) renal signs, (6) absence of cardiac symptoms, (7) fatal outcome, with signs of disease of the respiratory tract.

In general, lupus erythematosus disseminatus occurs more often in females than in males. With the particular type to which our case belongs, the predominance of females is especially striking. Of the twenty-three patients reported on by Baehr, Klemperer and Schifrin,[8a] twenty-two were females. Photosensitivity is a common symptom. It frequently converts a latent into a manifest disease or causes exacerbation. In many cases there is no history of exposure to the sun, indicating that this cannot be a necessary factor. However, the frequency of photosensitivity has suggested a relationship to porphyrinuria. No studies along that line were made in our case. Search for porphyrin in the urine was made in several of the cases reported by Baehr, Klemperer and Schifrin, and the results were negative.

Operative procedures, trauma and injections of tuberculin have precipitated attacks of lupus erythematosus disseminatus or caused severe setbacks during the course of the disease. In our case the removal of a tooth seemed to produce such a deleterious effect. That is why one hesitates to remove foci of infection no matter how desirable that procedure seems to be on theoretical grounds.

The renal symptoms were indistinguishable clinically from those in any other acute or subacute form of glomerulonephritis with elevated blood pressure. The absence of clinical cardiac disease was definite. On only one occasion was there a change in the electrocardiogram, and this proved to be insignificant and ephemeral. At no time did the usual clinical examination of the heart show any abnormalities.

The concept of lupus erythematosus disseminatus as a systemic disease may be traced first by a critical survey of the literature [10] and second by a discussion of the particular type to which our case belongs. The reported cases demonstrate numerous and varied types of noxa and equally varied responses thereto. In Madden's [11] series of eight cases, such diverse conditions were present as (1) cutaneous symptoms in a child of 5 associated with disease of the sinuses, which improved with drainage of the sinuses and recurred when drainage was interfered with; (2) carcinoma of the stomach with multiple metastases to the

10. By critical survey is meant the selection of such data as bear on the problem. A complete review is not intended.

11. Madden, J. F.: Acute Disseminated Lupus Erythematosus, Arch. Dermat. & Syph. **25**:854 (May) 1932.

lungs, shown by autopsy in a case in which the condition had appeared typical clinically, and (3) the more usual picture of so-called rheumatic pains, infection of the respiratory tract and cardiac and nephritic lesions. Mook and his associates [12] reported thirteen cases. Nine patients died, and four could not be followed. Nephritis was found in the four cases in which autopsy was performed. The high incidence of inflammation of serous membranes was striking. "In ten of the thirteen cases involvement of the serous membranes was either proved or convincingly suggested." Karelitz and Welt [13] reported a case of dermatomyositis in which the diagnosis made prior to their examination was lupus erythematosus disseminatus. They stated that lupus erythematosus disseminatus is one of several cutaneous lesions which may be associated with dermatomyositis. Sequeira [14] reported a case of scleroderma associated with lupus erythematosus disseminatus. In the case reported by Volk,[15] the condition was associated with periarteritis nodosa. (Interestingly, Volk emphasized the probable independence of lupus erythematosus disseminatus and vascular damage.)

Streptococcic infection has been emphasized, particularly by Barber,[16] as of etiologic importance. This illustrates a common pitfall in the analysis of cases of lupus erythematosus disseminatus. With a disease of such protean manifestations, one may choose a single symptom or pathologic lesion and by emphasis on the one finding to the exclusion of others arrive at a false notion of the central facts of the disease. Surely in our case infection of the respiratory tract was a terminal event. In general, we have the impression that the susceptibility to infection in lupus erythematosus disseminatus is due to a gradual lowering or wearing away of resistance. In this connection it is interesting that the toxin which causes lupus erythematosus disseminatus has a predilection for mesenchymal tissue. Although the site of the formation of antibodies has not been established definitely, the reticulo-endothelial system is considered to be a heavy contributor to the production of antibodies.[17] Disease of connective or interstitial tissue, which comprises a considerable portion of the body, might compromise the organism's capacity for the production of antibodies

12. Mook, W. H.; Weiss, R. S., and Bromberg, L. K.: Lupus Erythematosus Disseminatus, Arch. Dermat. & Syph. **24**:786 (Nov.) 1931.

13. Karelitz, S., and Welt, S.: Dermatomyositis, Am. J. Dis. Child. **43**: 1134 (May) 1932.

14. Sequeira, J. H.: Brit. J. Dermat. **33**:298, 1921.

15. Volk, R.: Dermat. Ztschr. **53**:682, 1928.

16. Barber, H. W.: Brit. J. Dermat. **31**:186, 1919.

17. Gay, F. P., and others: Agents of Disease and Host Resistance, Springfield, Ill., Charles C. Thomas, Publisher, 1935, p. 358. Maximow, A. A.: Morphology of the Mesenchymal Reactions, Arch. Path. **4**:557 (Oct.) 1927.

and thus explain the peculiar susceptibility of the patient with lupus erythematosus disseminatus to intercurrent infection.

We present this as a possible explanation and not as a hypothesis for which we would adduce evidence. However, regardless of the validity of the explanation, the evidence indicates that infection of the respiratory tract, supposedly streptococcic, is an intercurrent event and not the essential cause of the disease.

One might extend almost indefinitely the list of conditions with which lupus erythematosus disseminatus is associated. After reporting a case in which the condition was secondary to pyonephritis, Scholtz [18] expressed this idea very well when he stated that the "theory of multiple and diverse pathogenesis" is most acceptable. MacLeod,[19] likewise, stated that "it is not a pathologic entity due to some specific cause, but rather a cutaneous symptom of a peculiar type which may be called forth by a variety of toxic or septic causes." Baehr, Klemperer and Schifrin [8a] expressed a similar point of view: "It would seem that the disease is conditioned not by the nature or severity of the local infection but by a peculiarity in the constitutional reaction of the host."

What is the significance of the histologic findings at necropsy? As far as the glomerular lesions are concerned, they account for the clinical renal symptoms. Moreover, the appearance of the involved glomeruli leaves no doubt that the renal pathologic picture is not that of glomerulonephritis. The type of capillary alteration in this case, as in most of the cases reported by Baehr, Klemperer and Schifrin, is unusual, being similar only to lesions found in eclampsia, but far more severe. Because of the lack of reaction and the final decay of the glomerular tuft, the conclusion has been reached that the lesion is degenerative. The lesions in the spleen are also vascular, but they involve a larger vessel unit and are different in type. Such variety of pathologic alterations makes it difficult to come to a clear understanding of their significance. Just one fact is available, and that is the presence of vascular lesions as the only conspicuous pathologic observation in this case as well as in those previously reported from this laboratory. The severity of these lesions varies greatly, and even in the present case, in which it was most striking within the kidneys and the spleen and less so in the heart, it can hardly account for the variety of symptoms and the peculiar clinical course. The vascular lesions, therefore, cannot be regarded as the all-explaining foundation of the disease; they are merely manifestations of an underlying pathologic process which in its progress may and frequently does lead to

18. Scholtz, M.: Lupus Erythematosus Acutus Disseminatus Hemorrhagicus, Arch. Dermat. & Syph. **6**:466 (Oct.) 1922.

19. MacLeod, J. M. H.: Lupus Erythematosus, Arch. Dermat. & Syph. **9**: 1 (Jan.) 1924.

morphologic changes of the smaller vessels. An analogy can best illustrate what we want to express: The intravenous injection of bacterial toxins may kill a rabbit quickly, and at autopsy no morphologic lesions are found. If a smaller dose is given, and particularly if the injection is repeated, the animal may die or survive, but at autopsy numerous small thrombi are found within the spleen, liver, adrenals and kidneys.[20] In both instances the experimental toxemia is responsible for the result; the vascular lesions are of significance only as evidence of the experimental toxemia and certainly do not account for the death of the animal. In the same way, the vascular lesions found in this and other cases of lupus erythematosus disseminatus are merely an index of an underlying cause which we have not yet learned to understand.

The relation between lupus erythematosus disseminatus and vascular damage may be clarified by studying its history. Libman [21] and Libman and Sacks [9] first called attention to the association of lupus erythematosus disseminatus and atypical verrucous endocarditis. Later, Baehr [22] demonstrated, in addition to the presence of endocarditis, that of diffuse vascular lesions and emphasized their importance. The same author reported cases of lupus erythematosus disseminatus in which there was vascular damage without cardiac lesions. This new alinement of facts implied that endocarditis was not a necessary or essential part of the picture of lupus erythematosus disseminatus, and it centered attention on the blood vessels. The glomerular vessels were particularly vulnerable, showing changes in eighteen of the twenty-three cases reported. However, in a few cases reported by Baehr, Klemperer and Schifrin, vascular lesions were present only in the skin. This seems particularly significant, for vascular lesions only in the skin could not account for the profound systemic reaction of a serious and usually fatal disease such as lupus erythematosus disseminatus. Finally, in a few cases autopsy revealed no vascular lesions, although the condition had been indistinguishable clinically from lupus erythematosus disseminatus with vascular lesions. Naturally this raises the question of the rôle played by vascular damage. Is it the essential lesion or is it part of widespread damage caused by the unknown toxic agent that produces lupus? In other words, is it just one manifestation of the unknown and essential underlying cause? The absence of vascular lesions in otherwise typical cases, in which the usual course is pursued until death, indicates that damage to blood vessels cannot be the sole or essential

20. Apitz, K.: Virchows Arch. f. path. Anat. **293**:1, 1934. Gerber, I. E.: The Shwartzman Phenomenon in the Kidneys of Rabbits, Arch. Path. **21**:776 (June) 1936.

21. Libman, E.: Characterization of Various Forms of Endocarditis, J. A. M. A. **80**:813 (March 24) 1923.

22. Baehr, G.: Tr. A. Am. Physicians **46**:87, 1931.

lesion. However, mesenchymal structures in general seem to be affected in lupus erythematosus disseminatus. Baehr, Klemperer and Schifrin and Mook emphasized damage to the synovial and serous membranes. In one case of clinically typical lupus erythematosus disseminatus, in which at autopsy no cardiac or vascular changes were noted, there were lesions in the serous membranes and in the interstitial tissue, the mediastinum. Possibly, therefore, the following somewhat broader hypothesis might satisfy the facts thus far accumulated: The unknown toxic agent in lupus erythematosus disseminatus shows a predilection for tissue of mesenchymal origin, affecting at times the heart and vascular system, at times the blood vessels only and in a few cases the interstitial tissue only. Indeed, as new facts accumulate, it may be shown that other parenchymatous structures are affected either directly or indirectly as a result of damage to blood vessels. The history of the changing concepts of other diseases illustrates how certain clinical or pathologic manifestations at first so dominated the picture that they assumed the dignity of disease entities. Later, when the etiologic agent was discovered, these supposed disease entities took their rightful place as varied manifestations of the toxic agent. The unknown toxic agent in lupus erythematosus disseminatus may be a new and distinct substance or it may be one or more of a number of common bacteria or their toxins. The latter assumption is the accepted one, and lupus erythematosus disseminatus is considered to be the reaction of a peculiarly susceptible constitutional state to one or more of the banal organisms or their toxins.

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Progress in Pediatrics

JAUNDICE IN CHILDREN

REPORT OF SIX CASES OF ICTERUS GRAVIS NEONATORUM

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(Concluded from page 154)

REPORT OF SIX CASES OF ICTERUS GRAVIS

In the literature on jaundice in the new-born many writers [40] stress the point that three types of jaundice are characterized in a varying degree by edema, anemia, jaundice, enlargement of the liver and spleen, the presence of numerous nucleated red blood cells in the peripheral blood and numerous extramedullary hematopoietic foci. Common to the three types is the observation post mortem of extramedullary islands of blood formation. In the past, if edema was the most prominent element, the condition was spoken of as congenital hydrops foetalis, or universal edema of the new-born; if jaundice was most marked, masking the underlying anemia, the term icterus gravis neonatorum was used, and if anemia was most prominent, congenital anemia of the new-born was the term used. If in addition to enlargement of the liver and spleen, together with jaundice and anemia, there were unusual signs of erythroblastic activity in the peripheral blood and extramedullary organs, the term erythroblastosis foetalis was used. All these conditions are interrelated according to the newest terminology. They are subdivisions of the general heading, erythroblastosis foetalis. The advisability of this classification will be discussed later. The relationship between these conditions is illustrated by table 1.[41]

It is not my purpose in this article, the central theme of which is jaundice, to consider congenital hydrops foetalis, which is characterized principally by edema in addition to anemia, hepatomegaly and splenomegaly. Infants with this condition usually are stillborn or die shortly after birth. Nor is it my aim to describe congenital anemia of the new-born, of which the dominant characteristic is anemia, with jaundice

40. (*a*) Blackfan, Kenneth D.; Diamond, L. K., and Baty, J. M.: J. Pediat. **1**:269, 1932. (*b*) Parsons, L. G.;Hawksley, J. C., and Gittins, R.: Arch. Dis. Childhood **8**:159, 1933. (*c*) Ferguson, J. A.: Am. J. Path. **7**:277, 1931. (*d*) Buhrman, W. L., and Sanford, H. N.: Is Familial Jaundice of New-Born Infants Erythroblastosis? Am. J. Dis. Child. **41**:225 (Feb.) 1931.

41. Hawksley, J. C., and Lightwood, R.: Quart. J. Med. **3**:155, 1934.

as a secondary symptom. I intend, rather, to describe illustrative cases of the familial and sporadic forms of icterus gravis neonatorum.

CASE 1.—S. B., a girl aged 3 days, was admitted to the Jewish Hospital on July 13, 1929, with the complaint of jaundice since birth.

Family History.—The father was 35 and well; the mother, 28 and well. The mother had had 3 other children. The first, a girl, became jaundiced on the third day. The jaundice lasted four or five days. After recovering from jaundice, the child was asthenic. Dr. Kopkik thought she had a paralytic stroke. She died at the age of 2 months and 26 days. The second, a girl, became jaundiced on the third day and died on the fifth day. The third, a boy, was never jaundiced. At the time of the patient's admission he was 10 years old and healthy. The patient was the fourth child.

There was no history of jaundice in an infant or an adult in the family of either of the parents as far as could be traced. There was no history of syphilis, tuberculosis or diabetes. The mother was well during pregnancy with the exception of a cold in the first month which lasted a few weeks, the highest temperature being 101 F. The parents' Wassermann reactions were negative.

TABLE 1 (from Hawksley and Lightwood [41]).—*Erythroblastosis Foetalis*

Erythroblastosis Foetalis	
Intra-uterine	Neonatal
(1)	(1)
With universal oedema = hydrops foetalis*	With severe jaundice and anemia = icterus gravis neonatorum
(2)	(2)
Without oedema*	With severe anemia and little or no jaundice = anaemia haemolytica neonatorum

* Often stillborn.

Present Illness.—The baby was born three days before admission, at 3 a. m. She was well and normal until the night before admission, when she showed a slight yellow tint and refused part of the evening feeding. Next morning she vomited five times, the last time showing some yellow color in the vomitus. The stools were light green; the urine, a normal color. There was no constipation or diarrhea until the morning of admission. The child did not cry, nor was she restless. She had no fever at any time.

Physical Examination.—The patient was a well developed infant with intense icterus of the skin and the visible mucous membranes. She appeared moribund. The anterior fontanel was slightly depressed. The ears, eyes, mouth and pharynx were normal except for jaundice. The thorax was normal. The heart and lungs were normal. The abdomen was soft. The spleen was palpable 1 fingerbreadth below the costal margin, while the liver was not felt. The genitalia were normal, as well as the extremities. The activity of the reflexes was diminished. The umbilical stump was still present, but there was no evidence of infection.

Laboratory Findings.—A specimen of urine was not obtained. The blood cell count was: hemoglobin, 93 per cent; red cells, 4,400,000, and white cells, 4,000. One smear (200 cells) contained: polymorphonuclear neutrophils, 1.5 per cent; polymorphonuclear eosinophils, 2.0 per cent; small lymphocytes, 84 per cent; monocytes, 7.5 per cent; myeloblasts, 2 per cent, and myelocytes, 3 per cent. There were 12 extruded red cell nuclei, 1 stippled red cell, 15 megaloblasts and 9 normoblasts per hundred white cells. The reticulation was 0.5 per cent. One megaloblast undergoing mitosis was seen. There were moderate anisocytosis and poikilo-

cytosis, marked macrocytosis and slight microcytosis. Polychromasia was 2 per cent. Hemolysis began with 0.44 per cent saline solution and was complete with a 0.32 per cent solution. The coagulation time was four and one-half minutes; the bleeding time, eleven minutes. The platelets numbered 130,000. The Wassermann and the Kahn reaction were negative. The icterus index was 110. The direct immediate bilirubin reaction was positive; the indirect showed 5 units. The blood showed no agglutinogen and no agglutinins. There was no clot retraction after twenty-four hours. No isohemolysis was present. A blood culture was sterile.

Clinical Course.—Sixty cubic centimeters of a 25 per cent solution of dextrose with 3 units of insulin was administered intravenously. The dextrose was given on the basis that the severe icterus might have been due to severe destruction of the liver. The insulin was deliberately given in a proportionately smaller amount in order that the deposition of glycogen in the liver might be facilitated. The child took feedings poorly. The temperature fell from 100 F. on admission to 95 F. eight hours later. The patient died ten hours after admission.

Autopsy.—There was a slight amount of yellow fluid in the peritoneal cavity. The posterior and inferior margins of the lower lobes of the lungs showed subpleural hemorrhages. On section, the pulmonary parenchyma appeared normal except for deep jaundice. Microscopically, a few of the alveoli showed a yellow granular exudate. As to the heart, pinpoint hemorrhages were present in the epicardium, due to antemortem puncture. The myocardium was jaundiced throughout. The right ventricle was somewhat thickened. Both the foramen ovale and the ductus arteriosus were patent. The ampulla of Vater was also patent. The spleen weighed 15 Gm. It had smooth surfaces and was bright red and soft. On microscopic examination, the pulp was seen to be the seat of extensive hemorrhages. The sinuses were obliterated, and the follicles were fewer and smaller than normal. A moderate amount of yellow-brown bile was present in the gallbladder. The ducts and the portal system were normal.

The liver weighed 100 Gm. It had a smooth and glistening surface. It was reddish brown and on section appeared normal. Microscopic examination showed marked dilatation of the intertrabecular capillaries, with consequent pressure on and destruction of some of the liver cells. Scattered throughout were small areas of hemorrhage. Hematopoietic foci were abundant. The Kupffer cells showed no abnormalities. The portal spaces were normal. The bile ducts and capillaries were not distended. There was no evidence of accumulation of bile in the liver. The kidneys were normal macroscopically and microscopically. The urachus was normal. In regard to the bones, the femur showed no abnormality either grossly or microscopically. The brain weighed 350 Gm. and was markedly jaundiced. The pia showed gray thickenings about 1 mm. in diameter at several points in the lateral aspects of the brain.

Anatomic Diagnosis.—The anatomic diagnosis was (1) icterus, (2) congestion and edema of the brain and (3) congestion, hemorrhage and focal necrosis of the liver.

This case is an example of the familial form of icterus gravis neonatorum for the following reasons: (*a*) familial history, two previous children having died from jaundice, one at 3 months and the other at 3 days; (*b*) early appearance of intense jaundice, on the second day; (*c*) rapid, dramatic development of symptoms, with death on the third day; (*d*) palpable spleen; (*e*) characteristic blood findings: 24 nucleated red cells per hundred white cells, moderate anisocytosis and

poikilocytosis, hemoglobin 93 per cent and red cells 4,400,000 (while these figures are high, they do not seem so in relation to the normal polycythemia which exists at birth); (*f*) positive direct (immediate) van den Bergh reaction and high icterus index, 110, and (*g*) postmortem observation of abundant hematopoietic foci in the liver and an increase in size of the liver and spleen.

CASE 2.—S., a baby girl of the same family as S. B., was admitted June 19, 1930, at the age of 2 days, with the complaint of jaundice.

Family History.—The family history was the same as that in the previous case.

History.—The child was born at home at full term. The weight was 7½ pounds (3,402 Gm.). No resuscitation was necessary. There was no cyanosis and she cried immediately, with a lusty cry.

Present Illness.—The child appeared perfectly well until the morning of admission, when the family saw the much dreaded and not unexpected yellow discoloration of the eyes. The child's skin gradually assumed the yellow color, until in only a few hours there was deep jaundice. There had been no other symptoms, no diarrhea, vomiting or convulsions. All the stools before admission had been black except one, which was greenish. The physician who attended the child at home thought there was some purpura around the cord on the day of admission.

Physical Examination.—The patient was well nourished and had intense jaundice of both the skin and the mucous membranes. There was no evidence of hemorrhages into the skin, but the scleral conjunctiva of the left eye showed a small hemorrhage. The mucous membranes were of a good color. The extremities moved freely and were cold to the touch. The child cried vigorously. The respirations were rapid and regular. No deformity of the head was present. The fontanel admitted one finger. There were no areas of softening. The eyes were normal with the exception of a hemorrhage into the left sclera. The ears, nose, mouth and pharynx were normal. The chest was not abnormal in structure. The heart and lungs were normal. The abdomen was full. No distention was present. The appearance of the umbilicus was good, with no evidence of infection. The liver was palpable 1½ fingerbreadths below the costal margin, while the spleen was not felt. No masses were palpable. The reflexes were active. There was no involvement of the cranial nerves. No glandular enlargement was present. The epitrochleas were not palpable.

Laboratory Findings.—A blood culture gave negative results. The Wassermann and the Kahn reaction were negative. The icterus index was 75. The direct (immediate) bilirubin reaction was positive; the indirect showed 7.8 units. Examination of the blood showed: erythrocytes, 6,400,000; hemoglobin, 90 per cent; platelets, 300,000; color index, 0.70; coagulation time, eight minutes and fifty seconds; bleeding time, fifteen seconds; polymorphonuclear neutrophils, 94 per cent; band forms, 21 per cent; polymorphonuclear eosinophils, 1 per cent; myelocytes, 2 per cent; metamyelocytes, 3 per cent; abnormal cells, none, and reticulocytes, 2 per cent. A fragility test showed that hemolysis began with a 0.42 saline solution and was complete with a 0.28 per cent solution. There was no autoagglutination and no autohemolysis.

Clinical Course.—The jaundice kept on increasing. Fifty cubic centimeters of blood was given by transfusion. The temperature was normal. The child died the day following admission, after the onset of marked dyspnea and cyanosis.

Autopsy.—Marked jaundice of the skin and the scleras was present. Adipose and muscle tissues were bile stained. A small quantity of yellow-green fluid was

present in the peritoneal cavity. The heart weighed 20 Gm. Over the epicardium, several minute petechiae were present. The myocardium was deeply jaundiced, and the endocardium was bile stained. The foramen ovale was patent. The ductus arteriosus was extremely wide. Microscopically, the heart was normal. The pleural surface of the lungs showed few areas of air-containing parenchyma. The cut section through the rest of the lung showed moderate atelectasis. There was bile staining of the tissue. No areas of consolidation were present. Microscopic examination showed congestion throughout, with moderate atelectasis. There was an area of consolidation in which the alveoli were filled with red blood cells and considerable pigment.

The liver weighed 110 Gm. The surface was smooth and the consistency firm. On section, marked jaundice was found, and the usual liver architecture was lost by diffuse clouding. No bile plugs were visible in any of the bile passages. The hepatic duct and the portal vessels were normal. Microscopically, the liver cells appeared pale and granular. The nuclei stained well. There was congestion throughout, with numerous hematopoietic centers. The gallbladder contained a moderate quantity of thick yellow bile, which could be expressed through the biliary ducts to the duodenum without difficulty. The spleen weighed 20 Gm. There was a moderate degree of congestion. The gray network of the organ was prominent. Microscopically, marked congestion was observed throughout, with hemorrhagic extravasation and pigmentation. The lymph follicles were small but well defined. The kidneys each weighed about 10 Gm. Their capsules stripped with ease, leaving smooth surfaces, which were bile stained. On section, the cut surface was found to be extremely jaundiced. The pyramids were marked off from the cortical tissue by zones of yellow-green. Microscopically, marked cortical congestion and granular degeneration of the tubular epithelium were seen.

The skeleton showed no gross bony changes, and the epiphysial line of a femur exhibited no abnormalities. The marrow of the femur was red, and a scant amount of it could be scraped out. There was only a slight amount of bone marrow in the ribs. On microscopic examination of the bone marrow, numerous nucleated red cells of various sizes and forms were revealed. The white blood cell element was normal. The scalp was edematous and bile stained. The meninges were normal except for a blood clot on the right vertical portion, which was the result of a sinus puncture. The brain was edematous and evidenced some flattening of the gyri as a result of the edema. There was profound bile staining of the cortical and cerebellar tissue, especially the latter.

The umbilical cord, examined microscopically, showed the presence of an organized clot. The spleen and the heart showed no spirochetes with Levaditi's stain.

Anatomic Diagnosis.—The anatomic diagnosis was (1) pulmonary congestion with red hepatization and (2) patent ductus arteriosus, with thrombus formation.

This case is another example of the familial form of icterus gravis neonatorum. The patient was the next child of the mother of the first patient. The points outside the familial history in favor of the diagnosis of icterus gravis are: (*a*) early appearance of the jaundice, on the second day, and its becoming intense within a few hours; (*b*) enlarged liver, palpable 1½ fingerbreadths below the costal margin; (*c*) positive direct (immediate) bilirubin reaction and the high icterus index of 75; (*d*) the occurrence of death on the third day, after the onset of marked dyspnea and cyanosis, and (*e*) degeneration of the liver cells as noted by their pallor and granular appearance, increase

in the size of the liver and spleen and the finding of numerous hematopoietic centers in the liver.

CASE 3.—S., a baby girl was delivered normally at full term, at 10 p. m. on June 10, 1932. On examination the next morning the child appeared well nourished and had a vigorous cry. The skin was very red. There was no general enlargement of the lymph nodes. The eyes were not observed. The lungs were clear and the heart was normal. The liver and spleen were not palpable, and the cord was clean. Deep reflexes were easily elicited. The next day at 4:40 p. m. 45 cc. of the mother's serum was injected into the buttocks. The following day the skin appeared jaundiced after pressure was applied to make the redness disappear. Otherwise the child was normal. On June 13 the jaundice seemed to be unchanged in degree. The child was maintaining its weight. The temperature was normal, the color good and the lungs clear. While the spleen was not felt, the liver could be felt 1 fingerbreadth below the costal margin. The cord, having a red edge, was about to drop off. There was swelling or induration at the site of injection of the serum. The scleras could not be seen. The stools were dark greenish black and semiformed. The injection of maternal serum was repeated.

Laboratory Findings.—Examination of the blood showed: hemoglobin, 130 per cent; red cells, 7,000,000; white cells, 4,800; polymorphonuclears, 45 per cent; lymphocytes, 45 per cent; monocytes, 1 per cent; eosinophils, 9 per cent; normoblast, 1; red cells, normal in shape, and platelets, normal by smear. On June 13 the blood findings were as follows: hemoglobin, 120 per cent plus (Dare); platelets, 160,000; white cells, 10,600; polymorphonuclear neutrophils, 53 per cent; polymorphonuclear eosinophils, 5 per cent; small lymphocytes, 33 per cent; monocytes, 8 per cent; erythrocytes, 7,000,000; color index, 0.85 per cent; bleeding time, one minute and thirty-five seconds; clot retraction, normal; tourniquet test, negative; coagulation time, eight minutes; microcytosis, 2 plus; hyperchromasia, 2 plus; reticulation, 0.5 per cent, and fragility test, within normal limits.

Clinical Course.—The intensity of the jaundice as judged by the skin reached its height on June 14 and then began to recede gradually. No bile was found in the urine. There had been frequent loose stools since birth. The child maintained her weight but showed no gain. By discontinuing the formula for twelve hours and giving a saline solution and dextrimaltose, we controlled the diarrhea. On discharge, the color of the skin was faintly icteric. The scleras were clear; the heart and lungs, normal. The liver was palpable 1 fingerbreadth below the costal margin, while the spleen could not be felt.

The condition of this child, the sixth to be born in the family that is being reported on, can safely be considered to have been icterus gravis, in view of the fact that four children in the family had already died from this disease. Obviously, the clinical course and the blood picture were modified by the fact that maternal blood serum was given before the appearance of jaundice. The only other findings pointing to the diagnosis of icterus gravis are the appearance of jaundice and the enlargement of the liver.

CASE 4.—B. C., a girl 2 weeks old, was admitted on April 5, 1932, with the chief complaint of increasing yellowness of the skin.

Family History.—The family history was negative.

Present Illness.—Delivery had been normal and spontaneous. The color was normal at birth. When the mother and child were discharged from a private sanatorium on the tenth day, the mother first noted that the infant's skin had a yellow tinge, which she admitted may have been present before. The color deepened progressively, but the child remained otherwise well until two days before admission, when she began to refuse feedings. There were no fever, vomiting or convulsions. The stools were yellow, never clay colored or black.

Physical Examination.—The child was well nourished but markedly jaundiced. There were no eruptions on the skin. The head was well formed and the fontanel open and flat. The eyes showed icteric scleras and conjunctivae. The pupils reacted to light. The ears and nose were normal, while the mouth showed an icteric mucosa but no injection. There was no deformity of the chest. The heart was not enlarged, and the sounds were of good quality. A systolic murmur was present over the precordium but was not transmitted. The lungs were normal. Abdominal examination revealed a soft spleen 2 fingerbreadths below the costal margin, while the liver was only slightly below the costal margin.

Laboratory Data.—Two specimens of urine showed bile (nitric acid test) but were otherwise normal. Examination of the blood showed: on April 5, hemoglobin 60 per cent, red cells 2,520,000, white cells 29,520, polymorphonuclears 51, lymphocytes 43, monocytes none, eosinophils 5, basophils 1 and, on smear, fragmented red cells; on April 7, red cells 1,860,000, polymorphonuclears 45, lymphocytes 38, monocytes 11, eosinophils 2 and, on smear, marked anisocytosis, diffuse basophilia, 1.5 per cent reticulocytes, 1 myelocyte and 3 normoblasts; on April 8, hemoglobin 32 per cent, red cells 1,700,000 and white cells 20,800; on April 11, hemoglobin 56 per cent, red cells 2,710,000 and white cells 9,600; on April 15, hemoglobin 60 per cent, red cells 2,930,000, white cells 10,200, polymorphonuclears 23, lymphocytes 53, monocytes 18, eosinophils 6 and smear essentially normal, with no normocytes and few reticulocytes. The refractive index was 1.3467; the icterus index, on April 5, 170; the direct immediate bilirubin reaction, positive, and the indirect, 20 units; a vaginal smear, normal; a blood culture, sterile; a culture of material from the nose and throat, negative, and a roentgenogram of the chest, on April 6, normal. The stool on April 8 showed a faint trace of urobilin and of urobilinogen. The urine contained no urobilin and traces of urobilinogen which were inestimable because of the small amount of urine. A supravital differential count was as follows: polymorphonuclears, 33 per cent; bands, 7 per cent; metamyelocytes, 52 per cent (9,200); late myelocytes, 2 per cent; early myelocytes, 7 per cent; eosinophils, 6 per cent (1,100); small lymphocytes, 23 per cent (4,100); monocytes, 19 per cent (3,400); reticulocytes, 35 per cent; normoblasts, 14 per cent (15 per hundred white cells; 3,150 per cubic millimeter), and megaloblasts, 1 per cent.

Clinical Course.—The temperature was consistently normal except for a drop to 96 F. after the transfusion on the fourth day. The weight on admission was 6½ pounds (2,948 Gm.). Feedings were taken well, without vomiting. Transfusion of 60 cc. of blood on the fourth day was followed by a progressive decrease in jaundice. On the child's discharge from the hospital, on April 15, no jaundice was present. Except for evidence of moderate anemia, the blood smear was essentially normal. (Eight months later the blood count taken in the dispensary was absolutely normal.) A systolic murmur was present over the precordium. The lungs were normal. The liver was 3 fingerbreadths below the costal margin, and the spleen, 1 fingerbreadth.

This sporadic instance of icterus gravis is classified with this group for the following reasons: (*a*) marked jaundice; (*b*) enlarged liver

and spleen; (*c*) presence of bile in the urine; (*d*) positive direct (immediate) van den Bergh reaction, and (*e*) the changes in the blood—the increase in the number of nucleated cells, the presence of early forms of the leukocyte series and the presence of marked anisocytosis and a diffuse basophilia.

CASE 5.—H., a girl, was delivered at 3:10 p. m. on Dec. 11, 1934, after a normal pregnancy. She was the second child; the first one was living and well. The first child never had jaundice. The patient weighed 6 pounds and 13 ounces (3,090 Gm.). On December 12 nothing abnormal was noted. The next day at 1 p. m. the nurse reported that the baby was nursing poorly and that she had moderate jaundice. The temperature was 99.6 F. A clysis of 75 cc. of a 5 per cent solution of dextrose and sodium bicarbonate was given. At 7 p. m. the baby was in a poor condition. She was cyanotic and had difficulty in breathing. Examination showed frothy, bloody sputum from the mouth and nose. The chest was full of moist râles. Fifty cubic centimeters of serum from the mother's blood was given. Stimulants were also administered, and the child was placed in an oxygen tent. In spite of the serum, the child died the same evening.

Laboratory Findings.—At 9:30 p. m. on December 13 examination of the blood showed: red cells, 1,780,000; hemoglobin, 50 per cent; white cells, 117,600; polymorphonuclears, 6 per cent; lymphocytes, 93 per cent; eosinophils, 1 per cent; many nucleated red cells; many abnormal white cells; poikilocytosis, and anisocytosis.

This also was a sporadic case of icterus gravis. Marked jaundice appeared on the second day, although, as in all the previous instances, the baby appeared perfectly normal at birth. Within a few hours from the appearance of jaundice alarming symptoms appeared. There were marked dyspnea and cyanosis, followed by death. The blood findings were characteristic: a low red cell count and hemoglobin content, a tremendous increase in the total nucleated cell count, with many nucleated red cells and abnormal white cells.

CASE 6.—C., a girl, was delivered Sept. 11, 1934. She was the third baby, the previous 2 being normal. The family history was unimportant. At birth she cried spontaneously. The color was pink, and the birth weight, 7 pounds (3,175 Gm.). Definite jaundice was first noted about thirty-six hours after birth. On the third day, well marked jaundice was present but the child did not appear ill. There was definite pallor of the skin and mucous membranes. No cyanosis was present. The spleen was abnormally firm, extending about 3 cm. below the costal margin. The next day the pallor seemed more marked. The infant did not appear ill. The spleen was now quite soft, extending about 2 cm. below the costal margin. A transfusion of 75 cc. of blood was given on the fourth day. There was no immediate reaction. Examination on the fifth day showed that the jaundice was still marked, but the child was not quite so pale. The abdomen was enlarged. The veins on the upper abdominal wall were dilated. This was probably due to the enlargement of the spleen and the liver. No other masses were palpable. The cry was vigorous. The extremities moved freely. The urine was yellow. The child was discharged on the tenth day, the subsequent course being unknown.

Laboratory Findings.—Examination of the blood on the third day showed 1,830,000 red cells and 32 per cent hemoglobin (Sahli); on the fifth day, 1,600,000

red cells, 28 per cent hemoglobin (Sahli), 16,000 white cells, 14 per cent segmented polymorphonuclears, 32 per cent band forms, 4 per cent juvenile forms and 52 per cent lymphocytes; on the fifth day (after transfusion), 2,550,000 red cells, 38 per cent hemoglobin, 16,850 white cells, 34 per cent polymorphonuclears, 57 per cent lymphocytes; 1 per cent monocytes, and 1 per cent eosinophils; on the sixth day, 2,100,000 red cells, 38 per cent hemoglobin, 17,000 white cells, 14 per cent band forms, 18 per cent segmented polymorphonuclears and 62 per cent lymphocytes, and on the ninth day (after a second transfusion), 2,900,000 red cells and 70 per cent hemoglobin.

This case is an instance of marked jaundice with underlying marked pallor. The spleen was enlarged. The red blood cell count and the hemoglobin percentage show marked anemia. While, unfortunately, the presence or absence of nucleated red blood cells is not stated, the increased total nucleated count must have included many nucleated red cells.

CLINICAL FEATURES

Icterus gravis neonatorum, as the cases observed by my associates and me at the Jewish Hospital show, may occur in familial or sporadic form. The pregnancy is usually normal, there being no toxemia, and the infant is delivered normally at term. While it has been stated that the first born is usually spared, this theory was not substantiated in the family cited. It is possible that the first born had a milder form, if one judges by the length of life, for she lived three months. She was asthenic and had what was considered a paralytic stroke. The jaundice is the most striking symptom. It is noted early. Sometimes this type is present at birth, but it generally appears within thirty-six hours, unlike physiologic jaundice, which as a rule, manifests itself after the third day. In 5 of the 6 cases cited, jaundice appeared on the second day, no definite statement being possible in 1 case (case 4). Once icterus appears, it quickly increases in intensity. The infants are usually drowsy and apathetic and rapidly and progressively become very ill. Within one day alarming symptoms supervene, and death takes place, with evidence of hemorrhage (case 5) or possibly of medullary failure (cases 2 and 3). The child in case 2, the fifth child in the family cited, was seen on the second day of life by a member of our attending staff and was carefully examined. Although she was jaundiced, her general physical condition was good. Next day death supervened, after cyanosis and dyspnea developed. There was a similar dramatic sequence of events in case 5. Spontaneous recovery is rare. In some cases of comparatively long duration in which the patient recovers, anemia that was previously masked by the intense jaundice is uncovered. In 1 of our cases, the jaundice receded before death (case 2). Anemia is not inevitable, however. One of our 2 patients who had the familial type and died had 4,500,000 red cells per cubic millimeter, and the

other, the usual polycythemia of the new-born, 6,500,000 cells. On the other hand, in 2 of our cases the count was less than 2,000,000 red cells.

In addition to the symptoms of jaundice, pallor, drowsiness and failure to gain weight, one finds on examination that the liver or spleen or both are enlarged, especially during the height of the hemolytic process. In each of the 12 cases cited by Blackfan and his co-workers,[40n] the spleen was enlarged. In 2 of our cases there was enlargement of the spleen and in 2 enlargement of the liver. In 1 both the liver and the spleen were palpable, while in another no definite statement was made. Purpura is not a conspicuous feature. One of our patients (case 2) showed a small hemorrhage of the scleral conjunctiva of the left eye. In case 5, frothy, bloody sputum from the mouth and nose was a terminal manifestation. The stools are colored with bile, and the urine shows the presence of bile.

LABORATORY DATA

Next to jaundice as a symptom, if not of equal importance, is the characteristic blood picture (table 2). One finds an increase in the nucleated red blood cell count far beyond physiologic limits. On the first day there should be no more than 5 nucleated blood cells per hundred white blood cells on examination by smear; on the second day, no more than 1, and on the third day, none. The increase is in normoblasts, erythroblasts and megaloblasts, as well as in reticulocytes. Megaloblasts are the direct derivatives of the endothelium of the blood capillaries. They have a basophilic cytoplasm because of the scant amount of hemoglobin. The next cell is the erythroblast. It includes all the intermediate stages when the cytoplasmic basophilia of the megaloblasts is giving way to hemoglobin formation and therefore to acid-staining cytoplasm.[42] The normoblast is the cell of the common erythrocyte size with a pyknotic, or shrunken, nucleus. The nuclei then disappear, and the young erythrocytes, or reticulocytes, are formed. These are identified by a reticular network brought out by staining with cresyl purple. Next are the mature erythrocytes. Only three of our patients had an increase in nucleated red blood cells. As improvement in the condition occurs, the older cells disappear first. The red cell count varies; in our series it was between 1,780,000 (case 5) and 7,000,000 (case 2). The blood picture which usually obtains is that of hyperchromic anemia; that is, the diminution of red blood cells is out of proportion to the amount of hemoglobin. The color index is 1 or above. In 3 of our 6 cases the index was 1 or over.

The red blood cells have been described as showing, on smear, characteristic changes in size, anisocytosis, and variations in staining,

42. Sabin, Florence R.: Physiol Rev. **8**:191, 1928.

polychromasia. In the study of blood smears, we noted changes both in size and in shape. The characteristic cell has been described as a large cell, or macrocyte, which fits in with the findings of van Creveld[43] that the mean diameter of the red blood cell in icterus gravis is larger than that of a premature infant, which in turn is larger than that of an infant born at term, the last being still larger than that of an adult. The findings in icterus gravis as to the size of the cell have been corroborated by others.[41] Only 1 of our patients showed a marked increase in the size of the cells.

As for other blood findings, the leukocytes also increase in the early stages, myelocytes and myeloblasts being found, as well as band forms of polymorphonuclears, in the peripheral blood. We found no changes in the lymphocytic series, an experience corroborated by others. According to Blackfan, however, the lymphocytic series also shows early forms. The platelets have been variously described as increased, normal and diminished. According to some writers, they are definitely diminished. This diminution plus the tendency to an increase in the bleeding time may account for the tendency to hemorrhages. In 2 of the 3 cases in which the platelets were estimated, the number was diminished; in 1 of these cases, the bleeding time was increased to eleven minutes and the clot retraction was delayed.

In regard to other laboratory data, with the van den Bergh test in the 3 cases in which it was done, a direct immediate reaction was obtained and, of course, a markedly increased indirect reaction and an increased icterus index. The occurrence of a direct immediate reaction or, as is more characteristic, a biphasic reaction,[44] implies that there must be necrosis of the liver cells, with resulting disruption of the bile canaliculi. The urine shows an increase in urobilinogen as well as in bilirubin. In the 1 case in which we were able to obtain a specimen, bile was present. The stools are of normal color.

PATHOLOGY

A composite description of both autopsies and the findings of other authors reveal the following facts. As in all cases of jaundice, there is yellow staining of the various organs and serous membranes. Petechial hemorrhages, such as those noted over the epicardium in case 2, are not unusual. The dominant findings are in the liver. It was enlarged in both cases, the normal weight being 78 Gm.[40c] The characteristic finding, the one seen in sections of the liver in both

43. van Creveld, S.: Diameter of Red Blood Cells of Premature Infants and of Those Born at Full Term, Am. J. Dis. Child. **43**:337 (Feb.) 1932.

44. Abt, Arthur F.: J. Pediat. **3**:7, 1933.

TABLE 2.—*Results of Examination of the Blood in the Six Cases*

Case and Date	Red Cells	Hemoglobin Percentage	Color Index	White Cells	Differential Count, Percentage (200 Cells)	Smear	Platelets	Coagulation Time	Bleeding Time	Fragility, Percentage	Clot Retraction	Icterus Index	Bilirubin Test	Miscellaneous Data
1	4,400,000	93	1.1	4,000	Polymorphonuclear neutrophils..... 15 Polymorphonuclear eosinophils..... 20 Small lymphocytes.. 84 Monocytes..... 75 Myeloblasts..... 2 Myelocytes..... 3	Extruded red cell nuclei, 12, and stippled red cell, 1, per hundred white cells; reticulation, 5%; megaloblast undergoing mitosis, 1; anisocytosis and poikilocytosis, moderate; macrocytosis, marked; microcytosis, slight	130,000	4½ min.	11 min.	44-32	None after 24 hr.	110	Direct immediate, positive; indirect, 5 units	Blood culture, sterile; agglutinogen, 0; agglutinen, 0; no isohemolysis
2	6,400,000	90	0.75	.....	Polymorphonuclear neutrophils..... 94 Band forms..... 21 Polymorphonuclear eosinophils..... 1 Myelocytes..... 2 Metamyelocytes..... 3	No abnormal blood cells; reticulation, 2%	300,000	8 min 50 sec.	15 sec.	42-28	.....	75	Direct immediate, positive; indirect, 7.8 units	Blood culture, sterile; Wassermann and Kahn reactions negative
3	7,000,000	130 plus	0.09	4,800	Polymorphonuclears 45 Lymphocytes..... 45 Monocytes..... 1 Eosinophils..... 9	1 normoblast; red cells, normal shape	Normal by smear							
	7,000,000	120 plus	0.85	10,600	Polymorphonuclear neutrophils..... 54 Polymorphonuclear eosinophils..... 5 Small lymphocytes.. 33 Monocytes..... 8	Hyperchromasia, 2 plus; microcytosis, 2 plus; reticulation, 5%	160,000	8 min.	1 min. 35 sec.	Within normal limits	Normal			
4 4/11	2,710,000	56	1.0	9,600										
4/15	2,930,000	60	1.0	10,200	Polymorphonuclears 23 Lymphocytes..... 53 Monocytes..... 18 Eosinophils..... 6	Red cells, essentially normal; no normocytes; rare reticulocytes								

4/ 5	2,520,000	..	1.2	29,250	Polymorphonuclears 51 Lymphocytes..... 43 Eosinophils..... 5 Basophils..... 1	Fragmented red cells	170	Direct immediate, positive; indirect, 20 units	Blood culture, sterile; urine, 2 specimens showed bile
4/7	1,860,000	..	0.90	.....	Polymorphonuclears 45 Lymphocytes..... 38 Monocytes..... 11 Eosinophils..... 2 Myelocytes..... 1 Normoblasts..... 3	Marked anisocytosis; basophilia; reticulocytes, 1.5%			
4/8	1,700,000	32	....	20,800 (corrected for nucleated red cells 17,700)	Polymorphonuclears 33 Bands..... 7 Metamyelocytes..... 3 Late myelocytes..... 2 Early myelocytes..... 7 Eosinophils (1,100).. 6 Small lymphocytes (4,100)..... 23 Monocytes (3,400)... 19	Nucleated red cells; normoblasts, 14; megaloblast, 1 (15 per hundred white cells, 3,150 per cu. mm.); reticulocytes, 35%			
11/16	4,800,000	82 (11.8 Gm.)	0.80	8,000	Polymorphonuclears 13 Bands 11% (1,900)... 24 Eosinophils (250).... 3 Small lymphocytes.. 46 Large lymphocytes (4,200)..... 6 Monocytes (1,500)... 19 Degenerated cells.... 2	Red cells, essentially normal in appearance; rare poikilocytosis			
5	1,780,000	50	1.40	117,600 (uncorrected)	Polymorphonuclears 6 Lymphocytes..... 93 Eosinophils..... 1	Many nucleated red cells; many abnormal white cells; poikilocytosis and anisocytosis			
6 9/14	1,830,000	32	0.80						
9/16	1,600,000	28	0.80	16,000	Polymorphonuclears, segmented..... 14 Bands..... 30 Juvenile cells..... 4 Lymphocytes..... 52	Moderate anisocytosis and poikilocytosis; moderate polychromasia; 2 nucleated red cells per hundred white cells			
9/17	7,210,000	38	....	17,200	Band forms..... 14 Polymorphonuclears, segmented..... 18 Lymphocytes..... 62				
9/20	2,900,000	70							

autopsies and the one described as occurring in the spleen, kidneys and other organs, although it was not demonstrated by us elsewhere than in the liver, is islands of blood formation. These are really a persistence of or a reversion to embryonic blood formation. These centers of hematopoiesis consist of erythroblasts situated about the periphery, generally, while in the center are still more primitive cells, with basophilic cytoplasm, such as megaloblasts. In addition to the early forms of the red blood cell series, primitive forms of the granulocyte series, such as myeloblasts, also occur, but not to so marked an extent. We have found degenerative changes in the liver cells, such as paleness of outline and granular changes, and also necrosis of the cells, probably a result of pressure by hematopoietic foci. The portal spaces are normal, and there is no blockage of bile ducts. Our subjects did not show a deposition of bile pigment in the liver cells or casts of the bile ducts. These have been described as occurring in patients who survive several weeks.[41] The same explanation holds for the lack of deposition of iron pigment. In addition to these changes, there was congestion throughout the liver.

As for the other organs, there was some thickening of the right ventricle. In the bone marrow there was an increase in the formation of red and white blood cells in 1 case, while in the other there was apparently no change. In a few necropsies after icterus gravis there have been found pigmentation and extensive necrosis of the ganglion cells of the basal nuclei and medulla, which had given rise to the entity kernicterus.[45] According to a recent survey of cases,[46] the following symptoms have been ascribed to kernicterus: drowsiness, apathy, convulsions, spasticity and medullary failure. It may be that in the first born of the family reported on, who was jaundiced and survived for three months with evidence of a "paralytic stroke," we were dealing with a sequel of kernicterus.

DIAGNOSIS

The importance of making a diagnosis as to the cause of jaundice in the new-born is made obvious by the fact that of a total of 59 patients with jaundice who were treated in the pediatric service in nine years, 26, or about 45 per cent, were in the neonatal period, that is, in the first month of life. The gravity of jaundice in the new-born, in the past at least, is indicated by the fact that 16 of 26 infants died, a percentage of about 60 per cent. Once one excludes the commonest form of jaundice in this period of life, physiologic jaundice, the prognosis is

45. Schmorl: Verhandl. d. deutsch. path. Gesellsch. **6**:109, 1904.

46. Zimmerman, H. N., and Yannet, H.: Kernikterus: Jaundice of the Nuclear Masses of the Brain, Am. J. Dis. Child. **45**:740 (April) 1933.

grave. The responsibility for making a prompt diagnosis is tremendous, for in icterus gravis the immediate giving of blood by transfusion or of blood serum intramuscularly is effective.

If the obstetrician is on guard instinctively or because of a history of familial jaundice, he may suspect the condition if he finds yellow-stained amniotic fluid, a large placenta or an infant covered with golden yellow vernix caseosa. In a group of cases in the Boston Lying-in Hospital, golden yellow vernix caseosa was a finding in every case.[47] Otherwise, the diagnosis is based on the following cardinal points: (*a*) a familial incidence of early and intense jaundice, (*b*) pallor, (*c*) an abnormally large number of nucleated red blood cells, (*d*) enlargement of the liver and the spleen and (*e*) the observation post mortem of extreme hematopoiesis in extramedullary sites.

Since the diagnosis of icterus gravis with erythroblastosis can be made with certainty only by the observation post mortem of widespread extramedullary hematopoiesis, it is important that it be differentiated clinically from other conditions that occur in the neonatal period. For practical purposes, I shall confine myself to the conditions which actually occur during this period of life as judged by our experience of nine years. An attempt will be made to describe the conditions in the order of their frequency and importance.

DIFFERENTIAL DIAGNOSIS

Before taking up each individual condition, it may be well at this point to consider the other conditions which are evidence of an erythroblastic process, congenital hydrops foetalis and congenital hemolytic anemia of the new-born. The three conditions characterized by erythroblastosis are looked on as three different degrees of the same process, the severest form being congenital hydrops, the intermediate icterus gravis and the mildest hemolytic anemia of the new-born.

Congenital Hydrops with Erythroblastosis.—Infants with congenital hydrops, or edema of the new-born, generally are stillborn or die shortly after birth. As the name implies, the condition is characterized principally by edema. Other symptoms are pallor, enlargement of the liver and spleen and typical extramedullary sites of blood formation. The symptom of jaundice is absent or slight. We had one such case during the past year, as the following brief summary indicates.

Baby E. G. was delivered normally at term. There was no history of toxemia during pregnancy. When the baby was born the respirations were irregular and gasping. She died half an hour later. Swellings of the neck and enlargement of the abdomen were noted. At postmortem examination these proved to be

47. Clifford, Stewart H., and Hertig, Arthur: New England J. Med. **207**:105, 1932.

due to edema of the tissues and of the ascites, respectively. The diagnosis was confirmed by the study of postmortem blood and autopsy observations. The blood cell count was: lymphocytes, 69 per cent; lymphoblasts, 1 per cent; mature polymorphonuclears, 14 per cent; band forms, 6 per cent; eosinophils, 3 per cent; eosinophilic myelocytes, 1 per cent, and myelocytes, 6 per cent. Examination by smear showed: macrocytes, 4 plus; microcytes, 3 plus; anisocytosis, 2 plus; poikilocytosis, 3 plus; polychromasia, 3 plus; normoblasts, 78 per hundred white blood cells, and megaloblasts, 17 per hundred cells. Chemical examination of the blood showed: sugar, 16 mg.; creatinine, 1.3 mg.; urea nitrogen, 36 mg., and uric acid, 6 mg. per hundred cubic centimeters. The anatomic diagnosis was (*a*) erythroblastosis of the skin, heart, intestines, liver, kidneys, uterus, spleen, pancreas and adrenals, (*b*) universal edema, (*c*) diffuse hyperplasia of the bone marrow and (*d*) pulmonary atelectasis.

Congenital Anemia with Erythroblastosis.—As to the other condition associated with erythroblastosis, congenital hemolytic anemia, the striking distinction is that anemia is the primary element, with jaundice secondary, while in icterus gravis, jaundice is the primary symptom and anemia the secondary one. Congenital hemolytic anemia, also, is characterized by an increase in nucleated red cells in the blood and particularly by an increase in the reticulocyte count. Anemia is generally noted in the first twelve days of life.[48] Jaundice appears early or as late as the fifth week.[49] The majority of the patients recover spontaneously. The benefit from transfusion is striking. The infant whose case is described in the following paragraph, although discharged as the youngest child to have had acute hemolytic anemia of Lederer, may well be considered as having had congenital anemia of the new-born with erythroblastosis.

Baby E. G. was admitted at the age of 17 days. When she was taken home at 13 days, slight jaundice was noted. The stools were normal, and the urine was dark brown. She was a well developed infant, not in distress. Generalized jaundice was present. No hemorrhages or petechiae were noted. The liver and spleen were palpable 1 fingerbreadth below the costal margin. Study of the blood on admission showed: hemoglobin, 40 per cent; red cells, 1,600,000; white cells, 53,400; polymorphonuclears, 50 per cent; lymphocytes, 42 per cent; monocytes, 1 per cent; eosinophils, 1 per cent; basophils, 1 per cent; large monocytes, 2 per cent; myelocytes, 4 per cent; normoblasts, 12 per hundred white cells, and platelets, 250,000. The red cells stained poorly and were markedly broken up. Two days later, just prior to transfusion, examination showed: hemoglobin, 19 per cent; red cells, 848,000; white cells, 68,200; polymorphonuclears, 31 per cent; lymphocytes, 55 per cent; monocytes, 5 per cent; myeloblasts, 1 per cent; myelocytes, 4 per cent; metamyelocytes, 4 per cent; normoblasts, 20, and megaloblasts, 1 per hundred white blood cells; reticulation, 30 per cent; beginning hemolysis in a 0.6 per cent saline solution and complete hemolysis in a 0.32 per cent solution; some stippling

48. Ehrmann, Evelina W.: Anemia of the New-Born Infant, Am. J. Dis. Child. **37**:138 (Jan.) 1929.

49. Pasachoff, H. D., and Wilson, L.: Association of Universal Edema of the Fetus and Congenital Anemia of the New-Born, Am. J. Dis. Child. **49**:411 (Feb.) 1935.

of cells; extruded red cell nuclei and hyperchromia of the red cells; platelets, 240,000; bleeding time, two and one-half minutes; coagulation time, three minutes; Wassermann reaction, negative; icterus index, 150; direct (immediate) bilirubin reaction, positive, and indirect, 22 units. There was no fever. A transfusion of 60 cc. of blood was given. After transfusion the hemoglobin content rose to 46 per cent. The red cell count was 2,150,000 and the white cell count 22,500. Without further transfusion, the hemoglobin content on discharge was 62 per cent, the red cell count 3,350,000 and the white cell count 7,400. The number of nucleated red cells and the reticulocytes, as well as the number of abnormal white cells gradually diminished. The spleen became smaller, and the jaundice gradually disappeared.

Icterus Neonatorum.—Physiologic jaundice is the commonest condition from which icterus gravis is to be differentiated. It is usually mild, occurs on the third day or later and as a rule clears up within a few days. It is unlike icterus gravis in that beneath the jaundice is a pink rather than a pale skin. The liver and spleen are not enlarged, and there are no nucleated red cells in the blood after the third day. On the first day there may be, physiologically, from 5 to 10 nucleated red cells per hundred white cells. These are mostly normoblasts. In premature infants the number of nucleated cells may be higher. In icterus gravis, on the other hand, there may be 25,000 or more nucleated cells per cubic millimeter. Absence of nucleated red cells, however, does not exclude icterus gravis. The van den Bergh reaction in physiologic jaundice is indirect only, and no bilirubin is to be found in the urine. The prognosis is good. The jaundice clears up rapidly. Normally, then, physiologic jaundice provides no great difficulty in differentiation. It is in cases in which the jaundice appears earlier and lasts longer or is complicated by some other lesion, such as a cerebral injury at birth, that differentiation may give some difficulty, as illustrated by the following report.

Baby C. C. was delivered normally at full term. Jaundice was noted on the third day. On the following day the child vomited, was restless and had irregular breathing, with long periods of apnea. No cyanosis was present. She had one convulsion on that day and numerous ones on the following day. On physical examination, generalized jaundice was observed. The breathing was irregular. Pin-point subcuticular hemorrhages were present over the neck and shoulders. The liver was just palpable, but the spleen could not be felt. Laboratory examination showed: urine, normal; blood culture, sterile; bleeding time, forty-five seconds; coagulation time, two minutes and forty-five seconds; platelets, 340,000. On smear, one normoblast was found; otherwise the specimen was normal. No reticulocytes were present. Spinal puncture yielded yellow, clear fluid under normal pressure. The vomiting was controlled. The child gained weight, and at the end of the first week in the hospital the jaundice seemed to clear up. The next week the jaundice was more intense. The infant was discharged although slight jaundice was present, since she was doing well in every respect. The diagnosis at discharge was acute diarrhea with intoxication, icterus neonatorum and convulsions (unexplained).

Sepsis Neonatorum with Jaundice.—The next condition for differential study is sepsis neonatorum. We have had a total of 17 cases in the neonatal period, in 7 of which the infant had jaundice. Two infants beyond the neonatal period, 5 and 11 weeks old, respectively, also had jaundice. All the infants in this group died. In sepsis of the newborn, one may find anemia, severe hemolytic jaundice and many nucleated red blood cells. The main point of differentiation consists in the fact that in cases of sepsis with jaundice the infant is sick primarily with vomiting, diarrhea or fever or shows evidences of localization of an infection, for example, about the umbilicus. The jaundice comes later. In icterus gravis, however, the condition starts with intense jaundice in an apparently well child. The presence or absence of fever is no guide, for the temperature is often normal in sepsis in the newborn. Only one of our patients had a positive blood culture. It is to be remembered that the infant with icterus gravis may have a terminal infection which makes it difficult to differentiate the condition from primary septic jaundice with secondary changes in the blood. The following report illustrates the difficulties of diagnosis. In this case of sepsis there were not only jaundice, enlargement of the liver and erythroblastosis, but also a familial history.

Baby C. C. was the third infant in a family in which the first child had died at three weeks from jaundice due to sepsis arising from an infected umbilicus. The second child had jaundice for two days but recovered. The child under discussion became jaundiced on the second day after birth and failed to gain weight. For ten days before admission the stools were loose and green. There was no fever. Enlargement of the abdomen and edema of the vulva were noted on the day before admission. On examination, jaundice of the body, scleras and mucous membranes was observed. A purpuric spot was present over the left anterior part of the chest and in the left scapular region. The abdomen was tense, and the umbilicus, pouting. The liver was enlarged, reaching to 3 finger-breadths below the costal margin. It was palpable through a resistant layer, which felt as though it was possibly due to fluid. The spleen was not palpable. Our impression was that we were dealing with hematogenous peritonitis. The abdomen was tapped, and Staphylococcus aureus was recovered. The same organism was obtained from a soft, fluctuating mass over the left posterior parietal region. Examination of the blood showed: platelets, 190,000; polymorphonuclear neutrophils, 43 per cent; small lymphocytes, 40 per cent; myeloblasts, 1 per cent; myelocytes, 9 per cent; metamyelocytes, 7 per cent; poikilocytosis, moderate; macrocytosis, moderate; Howell-Jolly bodies, 2, megaloblasts, 3, and normoblasts, 9, per two hundred white blood cells; reticulation, 4 per cent; beginning hemolysis in a 32 per cent saline solution and complete hemolysis in a 28 per cent solution; icterus index, 60; van den Bergh direct immediate test, positive, and indirect, 9 units; bleeding time, two minutes; coagulation time one and one-half minutes, and clot retraction time, under thirty minutes. Examination of the urine gave a positive reaction for bile on one examination and a negative reaction on two others. The child died ten days after admission, the diagnosis being sepsis neonatorum.

Congenital Obliteration of the Bile Ducts.—The main characteristics are jaundice, generally dating from birth, clay-colored stools and an enlarged, hard liver. The jaundice is progressive and intense. The clay-colored stools and the hard liver, together with the absence of nucleated red blood cells, serve to differentiate this condition.

Prematurity with Excessive Hemolysis.—Premature infants may have a jaundice that appears earlier, is more intense and lasts longer than the physiologic variety. Associated with it one may find pallor, anemia and a nucleated red cell count beyond the normal physiologic limits as given previously. Usually, premature infants with excessive hemolysis are less ill than infants with icterus gravis and do not show splenomegaly. Also, infants with erythroblastosis born prematurely are apt to be jaundiced at birth and to have severe and early anemia. Of 9 premature infants studied post mortem after from seven to nine months of intra-uterine life,[40c] 3 showed no evidence of hematopoietic activity in the liver. In 6, there were a few areas of hematopoiesis, consisting of hemoglobin-containing cells which appeared to be normoblasts. In erythroblastosis in infants born at term, on the other hand, there is marked extramedullary hematopoiesis with every type of embryonic cell. In spite of the distinctions given, it is often difficult to say where prematurity with jaundice due to excessive hemolysis ends and icterus gravis begins. A recent case not included in the preceding series, of which the report follows, is probably a case of icterus gravis with erythroblastosis in a premature infant, but there is room for argument because no standards for blood findings at the various ages of prematurity exist.

Baby S. was born on March 7, 1935, after a seven and one-half month pregnancy. The mother had pyelitis during pregnancy. When the child was born the color was good and the cry was spontaneous. The weight was 4 pounds and 15 ounces (2,239 Gm.). The following morning the baby was intensely jaundiced. The general condition was poor. A transfusion of 20 cc. of whole blood was given. During the day the infant appeared listless and did not respond to stimuli readily. When he did cry, his cry was shrill and weak. He died the following morning. A red cell count showed 3,000,000 red cells. On smear, many megaloblasts, erythroblasts, normoblasts and extruded red blood cell nuclei and central achromia were observed.

Winckel's Disease.—We had 2 cases of this condition, in both of which treatment with transfusions was successful. The first case was reported by Kramer and Polayes.[50] The condition is characterized by intense jaundice, which generally begins from the fourth to the twelfth day [50] and leads to bronzing of the skin and mucous membranes, hemoglobin in the urine, severe hemolysis, with chocolate-colored discolora-

50. Polayes, S. H., and Kramer, B.: J. Pediat. **2**:482, 1933.

tion of the blood, and rapidly progressive anemia. The characteristics which distinguish it from icterus gravis are intense cyanosis and the occurrence of hemoglobin derivatives in the urine and the blood. The child whose case was reported had many megaloblasts and normoblasts in the peripheral blood and enlargement of the liver and the spleen. The second child had many nucleated red cells in the blood and from 4 to 25 normoblasts per hundred white blood cells, as well as enlargement of the liver and spleen.

Atresia of the Duodenum with Jaundice.—We had 4 cases of atresia of the duodenum, in 1 of which the infant had jaundice. There should be no difficulty in differentiating this condition from icterus gravis. The symptomatology is that of acute intestinal obstruction—early persistent vomiting and obstinate constipation. Gastric peristalsis may be evident, as well as dilatation of the upper part of the abdomen. Jaundice in these cases indicates obstruction below the papilla of Vater.

The preceding paragraphs describe our experience with jaundice in the neonatal period. Other conditions for differential diagnosis are mentioned in the literature, the most prominent ones being the following:

1. Congenital syphilis: In 48 cases of congenital syphilis in nine years, only 1 infant had jaundice, infectious cholangeitis at the age of 11 weeks. Congenitally syphilitic infants may have physiologic jaundice together with enlargement of the liver and spleen. Cases are reported not only with the finding of nucleated red cells in the blood but also with that of extramedullary hematopoietic foci in the tissues. The family history, the Wassermann test, roentgenograms of the long bones and examination of the tissues post mortem for spirochetes should serve to differentiate the two conditions.

2. Hemorrhagic disease of the new-born: Jaundice in these cases is not likely to be severe. The liver and the spleen are not enlarged, nor do nucleated red cells appear in the blood. We have found that hemorrhages in icterus gravis are infrequent except as a terminal event.

3. Congenital heart disease: This may give difficulty, especially in the absence of murmur, because it is accompanied by dyspnea, cyanosis and, if decompensation exists, enlargement of the liver. The absence of severe anemia and nucleated cells should serve for differentiation.

4. Erythroblastic, or Cooley's, anemia: This is a disease of later infancy and childhood. It is characterized by its occurrence in people of Mediterranean origin, by marked hyperplasia of the bone marrow and by tremendous enlargement of the spleen. The hyperplasia of

the bone marrow creates characteristic changes in the skull and long bones and in the facial bones gives rise to a mongoloid facies.

5. Familial acholuric jaundice: Cases have occurred in the first few weeks of life.[51] Microcytosis, with the red cells smaller than those of the adult, which in turn are smaller than those of the normal infant,[43] is characteristic. Coupled with this, the finding of an increase in the fragility of the red cells in a physiologic solution of sodium chloride and the same finding possibly for one of the parents, serves to distinguish the two conditions.

6. Leukemia: A superficial glance at an erythroblastosis blood smear may lead to an erroneous diagnosis of leukemia. The many nucleated red cells may be mistaken for small lymphocytes and the erythroblasts for lymphoblasts or myeloblasts. Cases of leukemia reported in infants may have been based on this erroneous interpretation.[40a]

PROGNOSIS

Icterus gravis, as the name implies, is a serious disease. Its mortality rate is between that of the uniformly fatal congenital hydrops and that of the rarely fatal hemolytic anemia. The only statistics available are those of Rolleston [52] and Hampson.[51]

Hampson, from a combined series of the two sets of data, gives a mortality rate of 80 per cent. Death within the first five days is generally due to medullary failure. In cases in which the child survives for a longer period, it may be due to anemia, toxemia, hemorrhage or intercurrent infection. Spasticity and convulsions may be indications of the particular form of icterus gravis known as kernicterus, in which there is involvement of the basal nuclei. In many cases of mental deficiency, spastic diplegia and athetoid movements in later infancy and in chilhood, the condition is probably the sequela of kernicterus from which the child recovered.[41]

TREATMENT

Working on the suggestion that the new-born infant's serum may lack some antihemolytic agent until the functional maturity of the liver is established, an agent which is present in the maternal blood or in any adult serum, Hampson [51] treated 18 infants with intramuscular injections of maternal serum, with 17 recoveries. The eighteenth child was seen late in the disease. Intramuscular injections of 5 or 10 cc. of serum were given daily, the bilirubin level of the blood being used as a guide. These were continued until the bilirubin level was 1 to 150,000. Hampson objected to the use of whole blood because red

51. Hampson, A. C.: Lancet **1**:429, 1929.
52. Rolleston, H.: Practitioner **104**:1, 1920.
53. Footnote deleted.

blood cells are absorbed with difficulty, giving rise to hematoma, and because he felt that the supplying of additional red blood cells for hemolysis would only aggravate the condition. On the basis of that theory, the child in case 3 was treated with serum. Two intramuscular injections were given, and the infant recovered. She was given 45 cc. of serum within the first twenty-four hours, before the jaundice appeared, for we knew that we were dealing with a family in which 4 infants had died of icterus gravis, 3 in the first few days. No success with either human blood or serum injected intramuscularly has been reported by others,[41] however. The present method of treatment is founded on the use of transfusions. Transfusions are to be given on the basis of from 10 to 15 cc. per pound (453 Gm.) of body weight if the red blood cell count is considerably below 4,000,000 per cubic millimeter. They are to be repeated until the red cell level is maintained at 4,000,000. The blood of either parent may be used. Additional therapy is the continuance of breast feeding, the forcing of fluids and the giving of dextrose to combat any existing dehydration.

ETIOLOGY

The cause of icterus gravis, involving as it does the general subject of erythroblastosis, has been the basis of many theories and a great deal of discussion. For that reason it has deliberately been left out of previous consideration. It is impossible to understand the theories attempting to explain the cause of icterus gravis without understanding the mechanism of physiologic jaundice and that of the intra-uterine formation of blood.

There have been numerous theories to account for physiologic jaundice. Those up to 1925 have been summarized by van Creveld.[54] More recently, a dozen theories have been listed.[55] It is beyond the scope of this article to discuss them, since to do so would involve detailed evidence of disproof. Of more benefit it is, then, to proceed with the established facts based on clinical and experimental data and with the resultant present concept of icterus neonatorum.

The fetus lives in a state of constant oxygen want, or relative anoxemia. If one studies the fetal circulation, one is impressed by the fact that only in one vessel, the umbilical vein, coming as it does from the placenta to the fetus, does pure oxygenated blood exist. That the placenta acts as the lung for the fetus was demonstrated as far back as 1876, by Zweifel,[56] who showed that the spectrum of oxyhemo-

54. van Creveld, S.: Icterus Neonatorum, Am. J. Dis. Child. **30**:240 (Aug.) 1925.

55. Franklin, Morris: Am. J. Obst. & Gynec. **22**:913, 1931.

56. Zweifel: Arch. f. Gynäk. **9**:291, 1876.

globin could be seen in blood from the umbilical cord before the child breathed through its lungs. In the rest of the fetal circulation there is an admixture of venous and arterial blood, the mingling taking place in the liver and the heart. As a result of this anoxemia, there is a compensatory increase in red blood cells, just as in congenital heart disease, the reaction of the heart to high altitudes, etc., there is polycythemia. Since a great demand is made on the blood-forming organs, which in the fetus are the liver and the spleen, before the full development of bone marrow at maturity, early cell forms, such as reticulocytes and nucleated red cells appear. There are also evidences of hurried maturation of the blood cells. The amount of bilirubin in the fetus increases during gestation, the premature infant having a lower bilirubin content than the infant born at term.[57] Since an increase in bilirubin is to be found in the fetus and hyperbilirubinemia is the basis of jaundice, the factors having to do with icterus neonatorum are obviously of antenatal origin. Events which take place during delivery or subsequently are of no primary importance in the causation of jaundice.

The findings at birth may be described as follows:

1. The bilirubin content of the cord blood is at least five times as great as that of the mother or of an older infant, never being less than 2½ units.[58] The amount of bilirubin in the blood increases after birth, reaching a maximum on the third or fourth day, and then gradually drops to a normal level. This holds true, of course, for the icterus index also. The bilirubin of the cord blood as well as of the blood of the new-born always gives an indirect reaction, thus showing that one is dealing with nonobstructive jaundice.

2. The cord blood hemolyzes readily. If it is allowed to stand in a test tube, hemolysis takes place readily whether the corpuscles are in contact with the serum or whether the serum is replaced with physiologic solution of sodium chloride. Adult blood will not hemolyze when treated in the same manner.[58]

3. The oxygen content of the fetal blood is low. Further evidence that the fetus lives in a relative state of anoxemia has been produced by a comparison as to the oxygen saturation and capacity of the fetal arterial blood, which is the blood taken from the umbilical vein, with the blood from the radial artery of the mother. Maternal blood is within normal limits, while the blood of the fetus shows a diminished oxygen saturation. This is further evidence of the placenta's being a poor respiratory organ as compared with the postnatal lung.[58a]

57. Hampson, A. C.: Lancet **1**:429, 1929.

58. Goldbloom, Alton, and Gottlieb, R.: Icterus Neonatorum, Am. J. Dis. Child. **38**:57 (July) 1929.

58a. Goldbloom, Alton, and Gottlieb, R.: J. Clin. Investigation **9**:139, 1930.

4. Polycythemia is present at birth, the red cell count ranging from 5,200,000 to 7,000,000.[59] There is a rapid rise in red cells in the first six hours. The red cell count remains high during the first week and then gradually drops. The red cell picture is also abnormal at birth as to type, staining and size.

5. There are corresponding changes in the hemoglobin percentage, which were accurately determined by the oxygen capacity of the red cells by Lucas and his co-workers.[60] The percentage is highest on the first day of life.

6. The platelets are not altered.

7. Leukocytosis is present at birth, markedly increases in the first twelve hours and then begins to fall, reaching normal within five days. It is accounted for by the increase in the polymorphonuclears and metamyelocytes, or band forms. These are most common in the first eighteen hours. Abnormal cells of the lymphocytic series also occur, cells with sievelike structure as well as many small and large lymphocytes instead of medium-sized ones.

8. The fragility of the cord blood and of the peripheral blood of the infant is increased owing to the reticulocytes and the nucleated red cells. By making fragility tests on the unhemolyzed portions of the blood, it was found that the immature forms of red cells are more sensitive to saline dilutions than normal cells.

9. There is no bilirubin or urobilin in the first day's stool, or meconium. A little bilirubin appears on the second day, and from then on the amount gradually rises. Urobilin is absent from the stools for the first three days.[61]

10. The excretory efficiency of the liver of new-born infants is impaired owing to immaturity, as evidenced by the bromsulphalein test.[62] Infants more than 4 months of age excrete the dye as well as adults. Below that age, more and more of the dye is recoverable at the end of a half hour. During the first month from 20 to 30 per cent of the dye is recoverable.

With the foregoing facts in mind, one may attempt to link up the findings and see the basis for the theory that icterus neonatorum is a true nonobstructive, or hemolytic, jaundice. The fetus living in a

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59. (*a*) Goldbloom and others.[58] (*b*) Lippman, Hyman S.: A Morphologic and Quantitative Study of the Blood Corpuscles in the New-Born Period, Am. J. Dis. Child. **27**:473 (May) 1924.

60. Lucas, Palmer, and others: Blood Studies in the New-Born, Am. J. Dis. Child. **22**:525 (Dec.) 1921.

61. Snelling, Charles E.: J. Pediat. **2**:399, 1933.

62. Herlitz, C. V.: Acta pædiat. **6**:214, 1926.

state of relative anoxemia makes up for the oxygen want by an increase in the production of red cells, polycythemia. Since the fetus has no stores of mature red cells to throw into the circulation, early forms appear, such as reticulocytes and nucleated red cells. The bilirubin content and the icterus index rise. After birth there is no longer any need for the increase in the amount of red cells. As the cells are destroyed, the amount of bilirubin rises because of the released hemoglobin. If it rises high enough there is visible jaundice, that being a matter of degree only. The fragility of the cells becomes normal as the reticulocytes and the nucleated red cells disappear. That anoxemia produces polycythemia has been proved experimentally by the keeping of guinea-pigs in a state of low oxygen saturation. With the return to normal oxygenation, polycythemia disappeared, the icterus index rose and jaundice appeared.[63]

Icterus neonatorum is really the result of a physiologic adjustment on the part of the new-born infant to extra-uterine life. The temporary rise in the red cell and the white cell count in the first six hours is probably evidence of the sudden change in environment and the consequent sudden stimulation of the bone marrow.[59b] The jaundice belongs to the type of true nonobstructive, or hemolytic, jaundice because it fulfills the two cardinal requirements of that classification, hyperbilirubinemia and impairment of the excretory function of the liver. The hyperbilirubinemia has been repeatedly alluded to. The impairment of the excretory function due to immaturity is evidenced by dye tests,[62] by lowered levulose tolerance tests[61] and by the fact that although the bilirubin content in the blood is high in the first few days, very much above the usual level at which the normal mature liver removes bilirubin from the blood, no pigment products appear in the stool. Also, the greater immaturity of the liver in the premature infant accounts for the greater rise in bilirubin, with the greater persistence of jaundice, and for the fact that the icterus index remains high for a long time.

While the hemolytic nature of icterus neonatorum has been stressed, there must be other factors which in certain cases intensify the bilirubinemia and produce jaundice. Two of these may be mentioned: (*a*) Since the placenta is the respiratory organ of the fetus, it stands to reason that if there are infarctions, or areas of degeneration, in the placenta, which interfere with the small supply of oxygen, jaundice should be more prevalent in cases in which the placenta is of this type. Evidence along this line has been produced by a study of placentas and of the course of new-born infants.[64] (*b*) Since the blood volume of a

63. Goldbloom, A., and Gottlieb, R.: J. Clin. Investigation **8**:375, 1929.
64. Gottlieb, R., and Kearns, P. J.: J. Clin. Investigation **10**:319, 1931.

new-born infant is about one-twentieth or one-nineteenth of its weight, a baby weighing 7 pounds (3,175 Gm.) has a blood volume of 150 cc. It is known that about 100 cc. of blood can be expressed from a placenta and cord. It is obvious, then, that a delay in ligation of the cord sufficient to allow from 40 to 60 cc. of blood to enter the infant would increase the blood volume by from 25 to 40 per cent. The extra burden of blood with a high bilirubin content and with an increase in the number and fragility of the red cells on an immature liver should produce jaundice in a greater number of cases in which the cord is ligated late. Evidence to support this theory has been presented.[53]

Only two authors have attempted to connect physiologic jaundice with icterus gravis neonatorum both in its familial and in its sporadic form. An understanding of the attempt to relate these two conditions involves a reference to erythropoiesis in the embryo.

As one studies the formation of blood in the embryo, one finds that blood is formed in various tissues such as the liver, spleen and kidneys and the tissue beneath the skin. As maturity is reached and bone marrow develops, these extramedullary foci cease functioning. Extramedullary foci for the formation of blood are observed in full term children but especially in premature infants.[65] It is an abundance of these foci that constitutes the picture known as erythroblastosis. The finding of many early forms of red cells, that is, erythroblasts, normoblasts and reticulocytes, in excess of the physiologic maximum for the age constitutes the picture known as erythroblastemia. Abt [44] expressed the belief that in icterus gravis one is dealing with a persistence of this embryonic formation of blood.

Hampson,[51] who also correlated physiologic jaundice with icterus gravis, raised the following questions: If, as has been seen, bilirubin is increased during fetal life, why are babies not born jaundiced? What accounts for the marked increase in bilirubin in postnatal life? To explain these two facts, he postulated two suppositions: (*a*) In fetal life a great deal of the bilirubin is excreted through the placenta by the mother. Mention has been made in the literature of an increase in bilirubin in the mother's blood toward the end of gestation, but no specific data have been given. This is not an unusual supposition. While no doubt the fetal kidney functions, a good deal of its excretion is discharged by the mother. If this supposition is true, the rise in bilirubin in postnatal life is due to inability of the liver to assume excretion of the entire amount of bilirubin promptly. (*b*) The second supposition, and the one more stressed, is that during fetal life the maternal organism supplies an antihemolytic agent from its own liver, thus pre-

65. Parsons, Leonard G.: Arch. Dis. Childhood **8**:85, 1933.

venting undue hemolysis. After birth, the separation from this source of an antihemolytic agent accounts for the marked increase in hemolysis and the consequent formation of bilirubin until the infant's liver supplies an antihemolytic agent. Either view presupposes that the difficulty is with the liver. According to Hampson, icterus gravis results from a still further delay in the assuming of function on the part of the liver. Apart from these two authors, no one has attempted to correlate physiologic jaundice and icterus gravis neonatorum in recent literature.

Some of the theories, such as those attributing the condition to maternal toxemia,[52] sepsis [66] and syphilis, can be ruled out readily. A study of our cases rules them out as they have been ruled out by other writers. There have been other theories, such as congenital intoxication of the fetus through toxic maternal products,[67] insufficiency of the liver cells, which permits the entrance of bile into the blood,[68] and a form of new growth of erythroblastic tissue which corresponds to the leukoblastic tissue which is sometimes considered the cause of leukemia.[69] The present point of view as to the causation of erythroblastosis, by which, to reiterate, I mean the finding of active bone marrow and active extramedullary hematopoietic centers with or without erythroblastemia, centers about two divergent schools of thought. One group of writers, which may be considered the American group,[70] in which Blackfan and his associates are dominant, are of the opinion that one is dealing with a primary disturbance of the erythroblastic tissues, with hemolysis secondary to this cause. Another group, the British group,[71] consider hemolysis the primary disturbance, with erythroblastosis as a secondary phenomena. It is my aim, from a review of the literature and of our own cases, to present the arguments for and against each theory and to express a personal point of view.

The Theory That Erythroblastosis is the Primary Condition, with Hemolysis Secondary.—This theory has been presented most clearly by Blackfan, Diamond and Baty. They have shown that there is a relationship between congenital hydrops and icterus gravis, on the one hand, and between icterus gravis and hemolytic anemia of the newborn, on the other. As to the first two conditions, the following facts

66. Knopfelmacher: Ergebn. d. inn. Med. u. Kinderh. **5**:205, 1910.

67. Brüning, H., and Schwalbe, E.: Handbuch der allgemeinen Pathologie und der pathologischen Anatomie des Kindesalter, Wiesbaden, J. F. Bergmann, 1924, vol. 2, p. 1204.

68. Yllpö: Ztschr. f. Kinderh. **17**:334, 1918.

69. Woolley, P. G.: J. Lab. & Clin. Med. **1**:347, 1916.

70. Blackfan and others.[40a] Clifford and Hertig.[47]

71. Parsons and others.[40b] Hawksley and Lightwood.[41]

can be adduced: (*a*) Both have a familial incidence; (*b*) there are instances of both in which an enlarged placenta was found or the infant was covered with yellow vernix; (*c*) enlargement of the liver and the spleen and severe anemia with many immature nucleated cells in the blood have occurred in both; (*d*) the tissues differ very little histologically in the two conditions, and in the liver, spleen, kidneys and other organs show large areas of hematopoiesis, and finally, (*e*) those authors have reported a case in which both conditions occurred in the same family.

Similarly, a link has been shown between icterus gravis and hemolytic anemia of the new-born. In a case reported by the Blackfan group, all the findings of icterus gravis were present. As the process cleared, the hematologic findings were compatible with the diagnosis of hemolytic anemia of the new-born. Furthermore, a familial incidence has been reported for hemolytic anemia of the new-born.[72] Moreover, cases of hemolytic anemia have been reported in which there were areas of hematopoiesis similar to those seen in erythroblastosis foetalis.[73] Other writers have given support to the preceding views.[74]

According to this theory, then, the disease is a primary defect of the hematopoietic system, resulting, first, either in the failure of normal erythrocytes to maturate or in the overgrowth of immature forms; second, in the delivery of immature nucleated forms into the circulation and, third, in the increased destruction of erythrocytes. Other signs of the disease complex are considered secondary to dysfunction of erythrocyte production. The jaundice is at first hemolytic, and as the products of red blood cell destruction accumulate, the icterus increases because of functional insufficiency of the liver. Another factor in the jaundice is the addition of an element of obstruction due to pressure of hematopoietic foci on the liver cell cords, which results in necrosis and destruction of bile canaliculi.

There are definite objections to the theory that erythroblastosis is the primary disturbance in icterus gravis and the other related conditions. These are:

1. At postmortem examination nothing may be observed to explain the condition of familial icterus gravis, the changes being similar to those of physiologic jaundice.[75]

2. Cases of congenital hydrops and of congenital hemolytic anemia have been reported in which there was no erythroblastemia.[49]

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72. Ecklin, T.: Monatschr. f. Kinderh. **15**:425, 1919.

73. Susstrunk, G.: Ztschr. f. Kinderh. **38**:586, 1924. Schleussing: Verhandl. d. deutsch. path. Gesellsch. **21**:371, 1926.

74. Ferguson.[40c] Buhrman and Sanford.[40d]

75. Hampson, A. C.: Guy's Hosp. Rep. **78**:199, 1928.

3. In our 3 cases of icterus gravis in one family there was no increase in nucleated red cells in the blood. Other cases have been reported in the literature [76] in which the nucleated red cells did not increase.

4. The presence of an increased number of nucleated red cells has been reported in other conditions: (*a*) congenital syphilis,[47] (*b*) sepsis (case reported under the heading "Differential Diagnosis") and, (*c*) Winckel's disease (2 cases described under "Differential Diagnosis").

5. There hardly seems to be a dividing line between prematurity with excessive hemolysis resulting in jaundice and anemia and icterus gravis. This difficulty is evidenced by a case cited under "Differential Diagnosis."

6. Abnormally colored vernix caseosa and hypertrophy of the placenta are associated with other conditions.[47]

7. Specimens taken from fetuses that died of fetal erythroblastosis at different ages showed diminishing extramedullary erythropoiesis with increasing age.[77] This observation can be correlated with the gradual disappearance of nucleated red cells from the blood during the first three weeks of postnatal life.[51] It seems logical to expect that if erythroblastosis were the primary cause of this condition and the cause of death, extramedullary erythropoiesis would continue until an even later date.

8. While there are similarities between congenital hydrops and icterus gravis, on one hand, and between icterus gravis and hemolytic anemia, on the other, it is not logical to say that the first condition, which is uniformly fatal, is of the same group as the third condition, which is rarely fatal.

9. Definite standards are lacking by which to gage the significance of an increase in the nucleated red cell count. There are no definite reports of series of cases to show what the count is in such conditions as congenital obliteration of the bile ducts, Winckel's disease, sepsis and different stages of prematurity.

10. The frequent presence of embryonic erythropoiesis in premature and full term infants seems to be evidence against the assumption that these cells are so abnormal that they can initiate hemolysis and its effects.

11. Finally, I quote Parsons: [65]

> The erythron in infancy is anatomically even more widely spread than in the adult, because although the change over from the embryonic depôts of blood

76. Hart, A. P.: J. Canad. M. A. J. **15**:1008, 1925. Greenwald, Harry M., and Messer, William: Am. J. M. Sc. **174**:793, 1927. McClure, E.: Ztschr. f. Kinderh. **1**:86, 1931.

77. Hawksley, J. C., and Lightwood, R.: Proc. Roy. Soc. Med. **26**:1368, 1933.

formation occurs during the later months of gestation, this change is gradual and blood formation continues to take place in the shafts of the long bones, the flat bones, the liver, spleen and lymphatic tissues throughout the early months of postnatal life.

Here then is one authority who has considered the process a normal one.

The Theory That Hemolysis is Primary, with Erythroblastosis Secondary.—The British writers [78] have advanced the theory of primary hemolysis strongly for the following reasons:

1. Not all infants with congenital hydrops have erythroblastosis; this is evidence that erythroblastosis can only be a concomitant feature and not the cause of the disease.

2. It is hard to conceive that in a child apparently born normal profound anemia will develop within a day or two if hemorrhage or hemolysis has not taken place.

3. As a result of studies on the mean diameter of red blood cells, van Creveld [43] showed that the mean diameter of the red cells in premature infants, which is normally greater than that of full term infants, falls much more rapidly to approximate the adult size. The more rapid fall has been interpreted as a sign of the increase in hemolysis known to occur in premature infants. In icterus gravis, van Creveld found the fall in mean diameter to be still greater, thus implying a greater degree of hemolysis, an observation which has been corroborated.[41]

4. As has been mentioned previously, Hampson expressed the belief that some antihemolytic factor which had been supplied in utero by the mother is lacking in the new-born infant owing to a delay in hepatic efficiency. That serum will inhibit hemolysis he showed experimentally,[75] and its use has been the basis of successful therapy. This theory more readily links physiologic jaundice and prematurity with excessive hemolysis and jaundice to icterus gravis. The severe clinical picture found in icterus gravis would be explainable by a still greater delay in the supplying of this antihemolytic factor by the liver of the new-born child. Furthermore, the results of the products of destruction of the red cells, which have been proved experimentally [51] to be toxic, would tend to increase the severity of the condition.

The essence of this theory is that the hemolysis comes first and is severe and unchecked, the result being that the bone marrow and the extramedullary centers of hematopoiesis, which have barely, if at all, ceased functioning, are recalled into activity. Because of this stimulus there is an outpouring of nucleated red blood cells into the peripheral circulation, with resultant erythroblastosis.

78. Parsons.[63] Footnote 71.

Comment.—It may be well to analyze our cases at this point to see whether they substantiate the concepts of primary erythroblastosis or those of primary hemolysis.

CASE 1.—This patient was the fourth child in a family in which the first born was jaundiced in the first week of life. The jaundice in the first child cleared up, but the child remained puny and had symptoms of "paralysis," which may have been spastic diplegia, as evidence of kernicterus. Death took place when the child was 3 months old. The second child died on the third day of life of jaundice. Both were girls. The third child, a boy, was not jaundiced and was perfectly well. In the case under discussion, in which the child was the fourth in the family, the red cell count on the third day, the day of death, was 4,400,000 and the hemoglobin content 93 per cent. From one point of view, that of the physiologic standard for this period of life, which is from 5,600,000 to 7,000,000 red cells, anemia was present but not striking. The red cell count and the hemoglobin percentage certainly do not speak for severe hemolysis, particularly in view of the fact that the child died the same day. Death, however, was not necessarily due to anemia. The child may have died of medullary failure, a common cause of death in the first few days. No nucleated red cells and no reticulocytes were present in the blood. The only abnormal finding was 12 extruded red cell nuclei per hundred white blood cells. At postmortem examination, while numerous hematopoietic foci were found in the liver, they were not found elsewhere. The severe jaundice, the relative anemia of a hyperchromic type, with a color index of 1.1 and the increase in the indirect reaction for bilirubin and in the icterus index indicate that hemolysis was the dominant element in the picture.

CASE 2.—In this case, that of the fifth child in the family, the blood taken on the second day, the day before death, showed a red cell count of 6,400,000, 90 per cent hemoglobin and a color index below 1. There were no abnormal red blood cells. There was evidence of hemolysis, however, since the infant was markedly jaundiced, and the icterus index and the indirect bilirubin reaction were increased. Since reticulation was 2 per cent, the red cell count may already have represented compensatory polycythemia due to a primary unknown stimulus. At autopsy, hematopoietic foci were noted only in the liver. In the bone marrow there was an abundant increase in various nucleated red blood cells, with the white cells apparently being normal.

CASE 3.—The case of the sixth child of the family, a girl, is interesting for it is the first recorded case in which treatment was given before jaundice appeared in an infant born in a family with previous deaths from icterus gravis. It is hard to evaluate the meaning, then, of a blood count which was certainly normal for the age, 7,000,000 red blood cells and 130 per cent hemoglobin. One may even argue that the case was an example of physiologic jaundice.

CASE 4.—This was a case of the sporadic form of icterus gravis with erythroblastosis, of a slower progression of the disease and of a complete cure with transfusion. The infant had all the classic symptoms of anemia: enlargement of the liver and the spleen, many nucleated red cells and abnormal white cells, on smear, and an increase in bile pigment. There was even, as in cases 1 and 2, a positive direct immediate bilirubin reaction. Since the element of jaundice was not so dramatic in appearance as in the previous cases, it is hard to say whether this case cannot also be classified as an example of congenital hemolytic anemia of the new-born with erythroblastosis. It is difficult to differentiate between that

condition and the closely related icterus gravis neonatorum with erythroblastosis. The difficulty of differentiation as shown in this instance would certainly be an argument for the concept of this disease as given by Blackfan.

CASE 5.—Unquestionably, we were dealing with a sporadic case of icterus gravis with erythroblastosis. We had evidence of marked hemolysis and very marked erythroblastemia.

CASE 6.—This case also illustrates the relationship between icterus gravis and hemolytic anemia of the new-born. It definitely speaks for hemolysis as the primary cause. It is hard to conceive of a red blood cell count of 1,830,000 and 32 per cent hemoglobin on the third day without marked hemolysis. There were no nucleated red blood cells in the blood beyond the physiologic limits for the age.

While it is true that neither the theory of primary erythroblastosis nor that of primary hemolysis affords a full explanation as to the cause of icterus gravis because one has still to postulate a more fundamental cause that initiates either process, I am in favor of the view that primary hemolysis with erythroblastosis is a concomitant or secondary feature. The reasons for this belief are as follows:

1. In the normal adult, hemolysis of the red blood corpuscles plays no discernible rôle in the daily destruction of from 600,000,000 to 1,500,000,000 red corpuscles.[79] It does play a rôle in abnormal conditions and in a restricted number of diseases. Red corpuscles are destroyed primarily by fragmentation. They are broken down into constantly smaller fragments owing to the wear and tear of going through small capillaries. Phagocytosis plays a secondary part in the removal of aged and worn red cells. There is apparently a mechanism in the normal adult which does not allow hemolysis of the cells to take place.

2. In every new-born infant hemolysis is evidently going on. Physiologic jaundice is considered a form of hemolytic jaundice because of the proof, previously given, of hyperbilirubinemia and temporary insufficiency of the liver. Whether jaundice occurs or not, the argument that hemolysis normally takes place in the new-born infant is not affected, because the presence of visible jaundice depends only on the degree and rapidity of hemolysis and hepatic inefficiency.

3. One finds normally as a result of the relative anoxemia in which the fetus lives, erythroblastemia at birth. Nucleated red blood cells and reticulocytes occur normally. There are also other evidences of physiologic demands on the hematopoietic system. It is only when the numbers are excessive or when the increase appears beyond the third day that the process is considered pathologic. Again, it is only a question of degree in a fundamentally identical process. In fact, 1 case has been cited by

79. Wiggers, Carl J.: Physiology in Health and Disease, Philadelphia, Lea & Febiger, 1934, p. 42.

Lippman,[59b] in which there were 37.8 nucleated red cells per hundred white cells and yet no sign of prematurity or abnormality. It was considered a simple case of physiologic jaundice.

4. The appearance of nucleated red cells in the blood, which has been shown to be normal at birth and more marked in the premature infant, has been known to occur in other conditions. I have given examples of its occurrence in sepsis and Winckel's disease. The literature gives reference to its occurrence in congenital syphilis and even in congenital cardiac disease.[47] It may conceivably occur in other conditions. No data are available at the present time concerning the nucleated red cell count in other types of jaundice in the neonatal period.

5. Authentic cases of the erythroblastosis type are on record as well as our own 2 cases of icterus gravis, of which it cannot be said that extensive extramedullary hematopoiesis was observed post mortem.

6. Although one grants that congenital hydrops may show resemblances to icterus gravis and icterus gravis to hemolytic anemia of the new-born, it is still not logical to say that the uniformally fatal first condition has the same etiology as the second, which is rarely fatal.

7. The clinical symptoms associated in varying degrees with the three types of erythoblastosis are not in themselves primarily characteristic of any one condition. Anemia, pallor, edema and enlargement of the liver and spleen can be explained as results of the destruction of blood no matter what the cause is. The diagnosis of erythroblastosis rests on a histologic determination only. As yet too few autopsies in cases of jaundice in the new-born have been performed with the idea of erythroblastosis in mind to provide a basis for comparison.

8. By analogy, from the study of other diseases, one would logically expect a disease condition to be a perversion of a normal mechanism. One would expect icterus gravis to be a disturbance of or an increase in the severity of normal physiologic jaundice due simply to an increase in the hemolytic process. The more severe clinical picture of icterus gravis may be explained by the toxic effects of destroyed red blood cells, for which there is experimental evidence,[51] or by the secondary results of necrosis of the liver cells.

9. The theory of Hampson of the presence in utero of an antihemolytic factor of maternal origin which prevents the appearance of jaundice accounts for the failure of infants to be born jaundiced. A temporary hepatic insufficiency of the young organism, which often shows immaturity of other organs, would account for physiologic jaundice. Greater hepatic inefficiency would account for the increase in jaundice commonly seen in premature infants. One step further, still greater hepatic inefficiency would explain icterus gravis.

10. The theory that there is an antihemolytic factor lacking in the new-born has been the basis of successful therapy by the administration of serum or blood by transfusion in cases of erythroblastosis.

11. Finally, there is good authority [65] for the statement that extramedullary hematopoietic foci function normally in the early months of postnatal life. It does not seem likely that what is considered a normal condition should be the basis for such protean conditions as congenital hydrops and icterus gravis.

Leaving out of consideration the question as to whether the erythroblastosis is primary and the hemolysis secondary or vice versa, one naturally wonders what initiates the erythroblastosis or the hemolysis. The idea that a toxin is responsible has been suggested because, pathologically, there is necrosis of the liver cells and of the ganglion cells in the brain. How will that explain a familial basis for this disease? The possibly hereditary basis has never been investigated. Certainly this is not an unusual concept with diseases of the blood. One needs but pause to consider sickle cell anemia, with the peculiar property of sickling of the red cells; congenital acholuric jaundice, with primary small red cells, or Cooley's anemia, with its distribution among the races about the Mediterranean. If the cause of erythroblastosis is to be explained on a hereditary basis, how explain the apparently sporadic case? Of course, one may assume a mutation arising spontaneously in the germ cells. Work on the chemistry of the red blood cells, as outlined in a recent lecture by Cooley,[80] may shed additional light on the fundamental disturbances in the red cells.

SUMMARY AND CONCLUSIONS

I report 6 cases of icterus gravis neonatorum, including 2 autopsies.

These cases illustrate the following points, which have been ascribed to icterus gravis: (*a*) the familial as well as the sporadic form of the disease; (*b*) the early appearance of intense jaundice; (*c*) the rapid, dramatic development of alarming symptoms which lead to death within twenty-four hours; (*d*) a slower progression of the disease, with a cure by transfusion; (*e*) enlargement of the liver and spleen; (*f*) an increase in the number of nucleated red cells, as well as of the cells of the early leukocytic series; (*g*) the presence of bile in the urine; (*h*) a positive direct (immediate) van den Bergh reaction; (*i*) the postmortem finding of abundant hematopoietic foci in the liver, and (*j*) the therapeutic efficiency of blood serum given intramuscularly, as well as of blood administered by transfusion. On the other hand, I have shown that it

80. Cooley, Thomas B.: Cell and Plasma Lipids in Anemic States in Childhood. Tr. Am. Pediat. Soc. **47**:55. 1935.

is possible to have icterus gravis without an increase in nucleated red cells and without hematopoietic foci anywhere except in the liver and the bone marrow.

Every child born in a family in which there has been a previous death from icterus gravis should be treated as a potential patient, and blood should be given promptly. I have recorded, in case 3, the first instance known to us in which blood was given before the onset of jaundice to an infant in whom the condition was expected and in whom it apparently did not then develop.

I include a summary of recent work on the mechanism of jaundice.

The best classification based on the pediatric experience of my associates and me at the Jewish Hospital is proposed.

The mechanism of and the blood findings in physiologic jaundice are given.

Present theories regarding the nature of icterus gravis are discussed, and evidence is presented in favor of the idea that hemolysis is the primary disturbance and erythroblastosis a secondary phenomenon.

News and Comment

GENERAL

May Day.—The Children's Bureau of the United States Department of Labor has issued the following bulletin regarding May Day :

"The Children's Bureau sponsors May Day — Child Health Day activities at the request of the State and Provincial Health Authorities of North America and in accordance with the Congressional Resolution of May 18, 1928, authorizing the President to proclaim May Day as Child Health Day.

"Slogan: Health protection for every child.

"Objective: To promote the extension of year-round child-health services in every community, including services for physically handicapped children.

"Leadership: State May Day chairmen will be appointed by State health officers to plan the State Child Health Day program and to arrange for the cooperation of organizations concerned with child health.

State departments of education will be asked to cooperate by planning and directing school Child Health Day programs.

"Program: For community groups — (1) an evaluation of child-health services in the community based on a survey of existing child-health conditions and organization to promote child health, (2) the launching of new local child-health projects, and (3) exhibits or programs celebrating gains made.

For children — as a climax for the year's health program — festivals, athletic contests, programs, exhibits celebrating children's growth, vigor, and safety from health hazards.

State and local news stories, radio talks, and speeches.

"Requests for information on State programs or for further material should be sent to May Day chairmen in State health departments."

PERSONAL

Dr. Julian Graubarth, instructor in pediatrics at Tulane University of Louisiana School of Medicine, has been appointed physician in chief of the Jewish Children's Home and the Isidor Newman School, New Orleans. Dr. Graubarth succeeded Dr. L. R. DeBuys, who resigned.

CORRECTION

The following footnote was omitted from part 2 of the January 1937 issue of the AMERICAN JOURNAL OF DISEASES OF CHILDREN:

The publication of this supplement has been made possible by a grant from the Abraham-Jacobi Memorial Fund.

Abstracts from Current Literature

Anatomy and Physiology

REFRACTORY PHASE IN THE SMALL INTESTINE OF THE GUINEA-PIG. HANS MENGEL, Monatschr. f. Kinderh. **65**:88 (March) 1936.

Mengel presents a number of tracings proving that electrical stimulation of the filled small intestine of a guinea-pig causes contraction of both the longitudinal and the ring musculature. It is impossible to study the contractions individually. During the peristalsis the longitudinal fiber becomes refractory to further galvanic stimulation. In the empty small intestine electrical stimulation causes chiefly contraction of the longitudinal fibers. In these contractions there is no refractory phase to either galvanic or faradic current. The tone of the longitudinal fibers does not come under the "all or none" law.

GERSTLEY, Chicago.

CURVES OF GASTRIC CONTENTS IN INFANTS. WILLIAM STEIMANN, Monatschr. f. Kinderh. **65**:264 (April) 1936.

Steimann studied the effects of certain stimulants such as caffeine and histamine by fractional removal of the gastric contents. Histamine produces twice as much acid as does caffeine. The gastric acidity increases gradually during the first year. In nutritional disease the gastric acidity diminishes, emptying is delayed, and the gastric juice is decreased. In dysentery conditions are variable and may be either normal or as in nutritional disease. In acidosis the gastric juice is highly acid. Severe anemias do not lead to anacidity. In 100 children no achylia was found.

GERSTLEY, Chicago.

Biochemistry; Bacteriology, and Pathology

THE RELATIONSHIP OF ANTIANAPHYLAXIS TO ANTIBODY-BALANCE AND TO IMMUNITY. MARION C. MORRIS and J. BRONFENBRENNER, J. Bact. **31**:62 (Jan.) 1936.

Morris and Bronfenbrenner feel that antianaphylaxis is not due to an excess of circulating antibody. This was shown by injecting additional antibody into the circulation of passively sensitized guinea-pigs shortly before injection of antigen. Such animals were not protected against anaphylactic shock to any greater extent than sensitized guinea-pigs given intravenous injections of normal serum before being tested with antigen. It required smaller amounts of antigen to kill guinea-pigs which had received additional antibody than to kill guinea-pigs which had not received additional antibody.

The statement is also made that antianaphylaxis cannot be explained on the basis of a depletion of antibody, since desensitized guinea-pigs when resensitized fail to attain the same degree of reactivity as normal animals given the same amount of antibody. It was found that desensitization has no appreciable effect on the content of circulating antibody. Resistance of sensitized guinea-pigs to infection with virulent Friedländer bacilli, being dependent on the antibodies, was likewise shown to be unchanged by desensitization. The conclusions indicate that anaphylaxis and immunity are different manifestations of the same antigen-antibody reaction and that a state of antianaphylaxis is due to nonspecific changes and is independent of antibody balance.

STOESSER, Minneapolis.

Metabolism; Infant Feeding; Milk and Other Foods

DETERMINATION OF ETHYL ALCOHOL IN BODY FLUIDS. HENRY NEWMAN, J. Pharmacol. & Exper. Therap. **56**:278 (March) 1936.

Newman describes a very simple and accurate method which any one with a little training in chemistry can carry out. It is accurate to 1.5 per cent in specimens containing as little as 1 mg. of alcohol.

PILCHER, Cleveland.

INFLUENCE OF DIETARY RESTRICTION ON BODY CONFIGURATION. H. BAKWIN, R. M. BAKWIN and L. MILGRAM, Acta pædiat. **18**:305, 1936.

Measurements of thirty-three external dimensions of the body were compared in two large groups of infants who were identical in economic status and racial origin (Caucasian). The members of one group received regular medical supervision; those of the second group were unsupervised. The former group numbered 353 infants; the latter, 634 infants. Those infants whose development was supervised grew in length and weight as well as supervised infants from a better economic environment. The growth of the unsupervised infants in both length and weight was delayed. Accompanying this delay, statistically reliable changes in body configuration occurred; these changes were of the sort which have been described as characterizing the linear type of body build.

McCUNE, New York.

DISTURBANCE OF THE FUNCTION OF THE CEREBRUM LASTING SEVERAL DAYS AS THE RESULT OF SEVERE HYPOGLYCEMIA. C. E. RÄIHÄ, Acta pædiat. **18**:315, 1936.

The only common cerebral disturbance in diabetes mellitus is loss of consciousness, which may result either from severe ketosis or from insulin shock. Although the latter is ordinarily regarded as a benign complication of treatment, Priesel and Wagner stated that repeated attacks by hypoglycemia may lead to cerebral lesions and functional manifestations reminiscent of true epilepsy. Schleussing and Schumacher have reported the case of an 11 year old girl who exhibited symptoms of decerebration following a brief episode of diabetic coma, during which she was rendered repeatedly hypoglycemic by insulin therapy; the patient survived seventy-two days and then died.

The case presented in the present paper is that of a 13 year old girl who had had diabetes for about six months and who was doing well on a free diet and 64 units of insulin daily. On one occasion, because of an unforeseen reduction of her diet the usual quantity of insulin produced loss of consciousness. Through failure to recognize the hypoglycemic nature of the attack 120 units of insulin was given with therapeutic intent. Following this the child became deeply comatose, then crazed; clear consciousness was not recovered for five days, despite the fact that parenteral injections of dextrose and food taken by mouth caused the blood sugar content to return to normal within seven hours after the onset of the attack and to remain normal during the ensuing days.

Räihä speculates briefly on the pathogenesis of such manifestations as this.

McCUNE, New York.

AN APPARATUS FOR DETERMINING THE EXCHANGE OF RESPIRATORY GASES IN PREMATURE AND FULL-TERM INFANTS. C. E. RÄIHÄ, Acta pædiat. **18**:453, 1936.

This description of an ingeniously designed and constructed respiration chamber cannot be abstracted with profit. The assembly preserves many of the fundamental principles of the Benedict closed chamber. The consumption of oxygen is measured directly by means of a spirometer, as in the Regnault-Reiset apparatus. The

quantity of carbon dioxide produced is determined potentiometrically, using quinhydrone electrodes, by a modification of the technic described by Kauko. The accuracy of the latter determination is ± 2 per cent. The chamber yields satisfactory respiratory quotients when tested with an alcohol flame. A point of peculiar advantage is that the temperature of the system is under thermostatic control and can be elevated as high as from 30 to 35 C., thereby permitting premature infants to be studied without danger of causing their body temperature to fall. The paper is illustrated with diagrams and a photograph.

McCune, New York.

Vitamins; Avitaminoses

Studies of Vitamin C Excretion and Saturation. J. B. Youmans, M. B. Corlette, J. H. Akeroyd and H. Frank, Am. J. M. Sc. **191**:319 (March) 1936.

It has been found that normal human subjects excrete significant amounts of vitamin C in the urine. The usual daily excretion was observed to be relatively constant (from 30 to 33 mg.). Well nourished normal subjects were found to behave as though they had appreciable reserve stores of the vitamin, for when the vitamin was temporarily withheld from their diet they continued to excrete it for a time at an almost steady rate. When a large dose of the vitamin was given, an increase in the urinary excretion was observed. The vitamin C content of the urine was determined by the use of Tillmans' indicator, 2,6 dichlorophenol-indophenol, standardized every three days against a known solution of cevitamic acid. The microtechnic described by Harris and Rays (*Lancet* **1**:71, 1935) was used, with few exceptions. Disregarding those persons in the supposedly normal group whose diet was found to be questionable and taking those whose diets appeared reasonably adequate, the investigators found the daily excretion of vitamin C to be in the neighborhood of from 20 to 80 mg., values which correspond fairly well to those of Harris and Ray.

On this basis they tentatively adopted an excretion of 20 mg. per day as the lower normal limit of excretion in adults.

Of fifteen subjects whose diets were suspected of being inadequate in vitamin C, twelve excreted less than 20 mg. of the vitamin in the urine daily. Of sixteen normal controls whose diets supposedly were adequate, eight also excreted less than 20 mg. In the latter group subsequent inquiry suggested, for one or another reason, that there was a limited intake of vitamin C among those with low daily excretion of the vitamin. Of the thirty-one subjects, twenty-one excreted but a very small part of a large test dose of the vitamin in the twenty-four hours during which it was administered, indicating an apparent retention of a large amount and suggesting that the amount stored in the body had been small. In general, the tests of saturation gave results corresponding to the amounts daily excreted and to the probable dietary intakes of the vitamin. In four normal subjects it was found that following saturation the urinary excretion of vitamin C quickly fell to a low level when the subject was kept on a vitamin C-free diet. On the usual diet the fall was nearly as great and as rapid. With the subjects on their usual diet or a vitamin C-free diet, saturation was quickly lost after the administration of vitamin C was stopped, resaturation tests at intervals of two or three days showing an apparent retention of as much as 25 per cent of a test dose. The administration of small but varied doses (25 to 100 mg.) of vitamin C to unsaturated subjects had little effect on the daily urinary excretion of the vitamin. With the subjects on a vitamin C-free diet, the amount of the vitamin excreted in the urine in any given period following saturation is usually much less than the amount required to resaturate. For the present, a daily urinary excretion of vitamin C of 20 mg. and an excretion of 30 per cent of a test dose (about 600 mg. in adults) are suggested as the lower limits of normal daily excretion and saturation, respectively.

Comprehensive tables of the results are presented.

Henske, Omaha.

CALCIUM AND PHOSPHORUS STUDIES: XII. SIX YEARS' CLINICAL EXPERIENCE WITH VIOSTEROL IN THE PREVENTION AND TREATMENT OF RICKETS, TETANY, AND ALLIED DISEASES. D. H. SHELLING and K. B. HOPPER, Bull. Johns Hopkins Hosp. **58**:137 (March) 1936.

In contrast with other investigators, Shelling and Hopper obtained practically complete protection against rickets in 235 full term colored and 290 full term white infants with doses of viosterol in oil which varied between 5 and 20 drops daily. One drop of the preparation used contained 75 U.S.P. XI units or 225 international units of vitamin D. On the basis of this experience they conclude that the average prophylactic dose of viosterol which is to be recommended for full term infants is 5 drops a day (1,125 international units); this is comparable with the 3 teaspoonfuls of cod liver oil (1,200 international units) recommended by Park, by Hess and by Eliot. With doses of viosterol which varied between 5 and 20 drops a day 28 white premature infants were protected completely and 28 colored premature infants were protected satisfactorily. It is suggested that premature infants should receive about 20 drops of viosterol daily during the first four or five months of life; then the dosage may safely be reduced to 5 or 10 drops a day. In order to prevent nonrachitic osteoporosis, it is probably indicated that the diet of premature infants should be supplemented with dicalcium phosphate. The results of the administration of viosterol in twins and syphilitic infants were as gratifying as those obtained in premature infants.

Viosterol in amounts from 10 to 60 drops daily was used in the treatment of 134 patients with rickets of greatly varying severity. The average time for complete healing in the entire group was three months and three days; in 83.4 per cent of the infants healing was complete within five months. In a few with excessively severe infantile rickets a considerably longer period of time was required; in general, the time necessary for complete healing bore a closer relation to the original severity of the rickets than to the time at which treatment was instituted or to the dose of viosterol. It was found that healing could be accelerated by insuring that the diets of the patients contained sufficient amounts of calcium and phosphorus. In late rickets, i. e., active rickets which persisted past the end of the second year of life, the therapeutic response to viosterol was frequently slower than in the infantile type; large doses, sometimes as much as from 40 to 60 drops daily, were found to be particularly valuable in insuring and accelerating healing. The authors have not encountered personally a single patient with late rickets who could not be cured by adequate treatment with viosterol. Before operative treatment of rachitic skeletal deformities the bones should be at least partially hardened in order to prevent recurrence of deformities during the course of treatment. An alternative but still experimental method of rectifying rachitic deformities consists in the production of therapeutic osteomalacia with strontium carbonate; the authors have employed this procedure successfully in 9 cases. Viosterol is particularly useful in producing rapid healing of thoracic rickets, a condition which may jeopardize the life of the patient.

The ephemeral effect of calcium therapy in alleviating the symptoms of infants with tetany can be rendered permanent if the administration of viosterol is commenced a few days after the beginning of the treatment with calcium; in 21 cases the serum calcium level had risen well above the level in tetany within ten days after the institution of viosterol therapy. In this respect the action of viosterol is much more rapid than that of comparable doses of cod liver oil.

Viosterol is effective both in healing and in preventing the rickets of celiac disease. Since it augments the retention of phosphorus, it is contraindicated in renal rickets. Viosterol is to be used with caution in parathyroprival tetany and then only in conjunction with diets high in calcium and low in phosphorus. Experimental work with rats indicates that viosterol may increase the concentration of circulating lead in plumbism; when it is desired to deposit lead in the bones viosterol should be used cautiously and always with a diet high in phosphorus. Deleading is more safely accomplished by means of a diet high in

phosphorus and low in calcium without viosterol. For obvious reasons viosterol is ineffective in all of the numerous forms of achondroplasia which bear a superficial resemblance to rickets.

Information is entirely lacking concerning the fatal dose of viosterol for human beings. The poisonings which were reported earlier in conjunction with the use of vigantol were probably due to the mode of preparation, which resulted in a large admixture of "substance 248," or toxisterol. In their total experience the authors have encountered neither clinical nor anatomic evidence of injury to a single patient as the result of an overdose of viosterol.

In conclusion, it is denied that viosterol is only one-fourth as potent as cod liver oil; the comparative clinical efficiency of the two sources of vitamin D in terms of rat units is closer to 1:1.

A useful bibliography is appended. It is to be regretted that the influence of viosterol in preventing craniotabes does not come up for discussion.

McCUNE, New York.

SELECTIVELY IRRADIATED ERGOSTEROL. T. H. RIDER, GEORGE SPERTI, G. P. GOODE and H. G. CASSIDY, J. A. M. A. **106**:452 (Feb. 8) 1936.

The literature reveals that the clinical potencies of preparations of irradiated ergosterol are not as great as one would expect from comparative assays on rats of these products and cod liver oil. This finding may be due to the fact that irradiation of ergosterol with the full ultraviolet of the quartz mercury arc produces a multiplicity of products some of which are known to be inactive physiologically and others to be toxic without appreciable antirachitic activity. With a properly selected range of wavelengths ergosterol may be transformed almost completely into a fraction of high antirachitic activity free from degradative products. There is now available a product of selective irradiation which is a vegetable oil solution of the antirachitic factor, the potency of which has been adjusted to 10,000 U. S. P. X (Revised 1934) units per gram. Until clinical studies are made to establish the optimum dosage of this preparation—viosterol in oil, Sperti process—it is recommended that the doses advocated in "New and Nonofficial Remedies" be used.

BONAR, Salt Lake City.

REPORTS ON BIOLOGICAL STANDARDS: IV. THE STANDARDIZATION AND ESTIMATION OF VITAMIN A. E. MARGARET HUME and HARRIETTE CHICK, Medical Research Council, Special Report Series, no. 202, London, His Majesty's Stationery Office, 1935.

The first international conference for the standardization of vitamins, which was held in 1931, adopted a provisional standard for vitamin A "in terms of the biological activity of a sample of carotene." The belief that the standard could be improved was borne out when different investigators isolated several isomeric forms of carotene, including beta carotene. Furthermore, the crystalline carotene was found to be difficult to work with, and research was directed toward finding a proper solvent. The second international conference, held in 1934, adopted a solution of pure beta carotene as the permanent standard in terms of which units of vitamin A were in the future to be expressed.

The Medical Research Council and the Lister Institute jointly appointed a special subcommittee of the Accessory Food Factors Committee, and it was this team which did a great deal of the research on the standardization of vitamin A. Some of the researches were of minor, others of great, importance, and it was thought best to publish these investigations collectively as a record useful and important to experts in this field. Some of the reports have been published separately.

The forty-three page report deals with carotene as the international standard for vitamin A, proper oils as solvents and the relation of pure beta carotene to carotene; the spectrophotometric method of estimating vitamin A as compared

with the biologic assay, and the use of cod liver oil (U.S.P. X) as a subsidiary international standard for vitamin A. There is an appendix containing various protocols and the report of the second international conference on vitamin standardization.

SHAW, Evanston, Ill.

THE VITAMIN A AND D CONTENT OF THE LIVER OF NEWBORN INFANTS. K. U. TOVERUD and F. ENDER, Acta pædiat. **18**:174, 1935.

The senior author has published previous reports bearing on the increased maternal demand for calcium, phosphorus and iron during pregnancy. This paper is the second of a series which deals with the economy of the vitamins during child-bearing; the first contribution dealt with vitamin C. Specifically, the problem to be solved in the present work was whether the diet of the mother during pregnancy influences the amount of vitamin A and vitamin D present in the newly born infant.

Experiments on animals have shown that the reserve supply of vitamin A is conserved principally in the liver; the same condition is assumed to exist in human beings. The authors measured the concentration of vitamin A in the livers of ninety-seven newly born infants who died in the obstetric department of the University of Norway; the determinations were made by the British Pharmacopoeia commission's modification of the antimony trichloride method; following accepted precedent, the concentration of vitamin A was expressed in "blue units." The concentration of carotene was measured in a Lovibond tintometer by reference to a standard made of yellow glass. Since carotene also forms a blue color with antimony trichoride, it was occasionally necessary to apply a small correction for the presence of this substance to the values found for vitamin A. The concentration of vitamin A in the livers of the infants, expressed in numbers of units per gram of fresh liver tissue, ranged from 0.2 to 517 blue units. The lowest values were met with in the livers of those infants whose mothers had drunk the least milk and eaten the least vegetables during pregnancy; the highest concentrations were present in those whose mothers' diet had included ample quantities of these foodstuffs. There was no correlation between the degree of maturity of the infant and the concentration of vitamin A present in the liver at birth; actually, probably as the result of chance, the livers of premature and immature infants contained slightly more vitamin A than did the livers of full term infants. The values obtained for these Scandinavian infants were decidedly lower than those reported by Wolff, who found an average concentration of 73 blue units per gram of fresh liver for newly born Dutch infants. For comparison, Wolff's normal average value for adults was 245 blue units; Moore obtained a normal value of 235 blue units for adults in England.

The livers of forty-four newly born infants were examined for their content of vitamin D. A biologic method was used, namely, the ability of extract of the livers to produce healing of rickets in rats. Of the forty-four infants, twenty-four failed to show detectable amounts of vitamin D in the liver by this method. This is somewhat surprising, even though it is well recognized that the diet of Norwegian mothers is lamentably deficient in vitamin D. The livers of fifteen infants exhibited minimal concentrations of vitamin D; the livers of five showed from small to moderate amounts. The concentration of vitamin D was in direct relation to the amount of milk, eggs and, in one case, cod liver oil, which the mother had received during pregnancy. The fetal age of the infant exerted no influence on the concentration of vitamin D present in the liver.

MCCUNE, New York.

STUDIES OF HYPOVITAMINOSIS A: I. QUANTITATIVE INVESTIGATIONS OF THE RESORPTION OF VITAMIN A IN A CASE OF CELIAC DISEASE. C. FRIDERICHSEN, Acta pædiat. **18**:377, 1936.

The biologic, colorimetric and spectrometric methods of measuring the concentration of vitamin A do not fully meet clinical requirements; quantitative

estimation of the degree of hemeralopia presented by patients suffering from lack of vitamin A has proved to be a valuable practical means of determining the severity of the vitamin deficiency. With the assistance of C. Edmund, Friderichsen has elaborated a technic for measuring the extent of the loss of power of adaptation to darkness which eliminates the need of cooperation on the part of the patient; hence it is applicable to infants and young children. It consists in determining the minimum quantity of light which will produce an oculomotor reflex in patients who have been confined for some time in total darkness. The precise details of the test will be published in a forthcoming issue of *Acta pædiatrica.*

The method of examination was applied to a 7 month old infant with celiac disease. During the early stages of the illness the power of accommodation to darkness remained pathologically low despite the administration of a diet rich in carotene, which also contained a considerable amount of fat. No improvement was obtained when the patient was given for two weeks daily about 11,000 units of vitamin A in concentrated form. Striking clinical improvement and rapid recovery of normal power of adaptation to darkness were noted when the infant was given 500 Gm. of human milk daily. At the same time certain hyperkeratotic lesions which had developed during the illness disappeared promptly.

Friderichsen concludes that the vitamin A contained in human milk is more readily absorbed than that derived from other natural sources and from artificial sources.

McCUNE, New York.

EXPERIMENTAL RESEARCHES INTO THE INFLUENCE OF FREEZING ON THE VITAMIN C CONTENT OF ORANGE JUICE AND MILK. K. LILLEENGEN, Acta pædiat. **18:** 392, 1936.

This is an account of a carefully conducted study of the effect of freezing on the vitamin C content of orange juice and milk as measured by the therapeutic properties of both fluids. The guinea-pig was used as the test animal; healing was determined by means of extensive histologic studies of the jawbone and teeth. The paper is amply illustrated by reproductions of microscopic sections.

By freezing and storing fresh orange juice and fresh unskimmed winter milk at —30 F. for about four weeks the biologic effect of the vitamin C in orange juice was decreased by somewhat less than a third and that of the vitamin C in milk by about a third.

McCUNE, New York.

Hygiene; Growth and Nutrition; Public Health

MEASURES RECOMMENDED FOR THE PREVENTION OF EXTERNAL AND INTERNAL CONTAMINATION IN CHILDREN'S HOSPITALS. I. HUSLER, Bull. Assoc. internat. de pédiat. prevent., 1935, p. 29.

The prophylaxis of contagious disease inside the building is a crucial problem of every children's hospital. This prophylaxis is automatically assured by proper planning of the hospital, but it also depends on a carefully thought out and adapted technic of prophylaxis to be observed by both physicians and the nursing staff.

Infections occurring in a hospital may be divided into four groups according to the chief mode of transmission inside the hospital.

1. Infections by way of the digestive tract. The principal ones of these are typhoid, paratyphoid and dysentery. The common measures of hygiene have almost abolished these diseases, apart from some unexplained dysenteric manifestations occurring in wards for infants.

2. Contact infections, direct or indirect: erysipelas, gonorrhea, syphilis. Gonorrhea is particularly troublesome and is much more frequent as an infection in hospitals than is generally believed. The transmission of syphilis is almost unknown today.

3. Short distance infections. These are transmitted directly from child to child by droplets (whooping cough, diphtheria, scarlet fever, tuberculosis, various forms of influenza, quinsy and mumps). In these cases practical arrangement of the wards is very useful.

4. Long distance infections: measles, chickenpox, certain forms of influenza. These diseases create the greatest difficulties in hospitals.

General Prophylaxis.—The first step in hospital asepsis was made by Rauchfuss, who separated the different categories of infectious diseases. This separation must be carried out with the utmost strictness, and any slackening of the rule, such as that proposed by Schlossmann, must be looked on as a step backward. Separation alone is not enough to prevent a catastrophe when centers of infection have been formed. A further step is then necessary—the system of large wards must yield to one of small wards containing a limited number of beds, and large services must be split into a number of service units (Hutinel, Grancher and others); systematic isolation in individual cells should be deprecated. A third step is the establishment of a system of quarantine; this has its disadvantages, as it entails many complications, such as the duplication of all services and the moving of patients. This system can be modified by introducing localized quarantine within the unit, as practiced by Wieland and Husler.

The terrace system of building is not enough to prevent infection. Considerable risk is always caused by the admission center and the outpatient department. Protective measures concern chiefly the layout of the building and the staff. The problem of the outpatient departments has been usefully treated by Bessau.

Strict rules limiting the number of visits are absolutely essential, as are constant supervision of the staff, active and passive prophylaxis of all sneezing and coughing and an annual examination of the staff, particularly with regard to pulmonary trouble (roentgenologic or roentgenographic). Other measures are the raising of the minimum age for the admission of candidates for nursing and the compulsory isolation of all staff members who are not feeling well. As to the spreading of bacilli by healthy carriers and its prevention, strict application of general precautions is more to be recommended than any specific antibacillus campaign (such as the wearing of masks in case of need, and placing muslin curtains over the cots). Sliding panels are unreliable. Ventilation is important, especially the avoidance of strong currents of air (experiments in ventilation were carried on by Dzialoskzynski, and their application is given).

The formation of centers of infection owing to the "virulizaton" of the germs and their transmission by healthy persons are doubtless important, but this question has not yet been sufficiently studied.

Specific Prophylaxis.—Erysipelas: All persons suffering from this extremely contagious and serious disease must be immediately forbidden any contact whatever with babies and small children; they must be isolated in a room specially reserved for their use. In treating such patients india rubber gloves must be worn.

Gonorrhea: Measures for the control of this disease are constant inspection of body linen and of bedding and provision of individual bath and toilet articles, separate thermometers, and closed drawers for the girls. Isolation of all patients suspected of having this disease is necessary. India rubber gloves should be worn.

Diphtheria: Passive protection should be provided for children exposed to the risk of infection; bacteriologic inspection should be made to prevent late contagion, and, according to Schick, eventually separation of convalescent patients in different stages should be made.

Scarlet Fever: This disease may be controlled by sufficiently protracted isolation, "fresh air quarantine" for all children sent home to prevent return of infection and, according to Pospischill and Weiss, separation of convalescents in different stages.

Whooping Cough: First and foremost, the patient must be protected against other infections.

Tuberculosis: Necessary measures include the strict separation of patients in whom the condition is active and the isolation of children under 4 years old who react positively and negatively to tuberculin.

Measles: Besides general measures of isolation and prophylaxis, a supply of convalescent serum is necessary.

Chickenpox: Great difficulties are presented by this disease. Husler recommends the system of prophylaxis proposed by Birk (boxes, masks, careful ventilation of the wards, etc.).

Strict prophylaxis inside the hospital prevents transmission of infection so far as it abolishes serious risk of contagion. The avoidance of all dissemination and multiplication of germs is impossible, however. AMESSE, Denver.

VACATION COLONIES IN THE LOW COUNTRIES. A. A. KOOPAL, Bull. Assoc. internat. de pediat. prevent. **3**:8, 1935.

In 1876 a Swiss clergyman, the Rev. W. Bion, started the first holiday camps. This example was followed by many countries, among them Netherlands, in 1883. It was only in the early part of the twentieth century, after the foundation of the "Centraal Genootschap voor Kinderherstellingsen Vacantiekolonies" that the number of holiday camps in Netherlands increased rapidly.

In 1907 and in 1909 Professor G. Scheltema, of Gröningen, laid down certain essential principles that acknowledged the existence of fundamental problems in adolescence. The name holiday camp has gradually been changed to health camp, and it became customary to distinguish two kinds: (1) that which implies the common group treatment during five or six weeks, and (2) that which implies more individual care for at least two months.

After 1920 a state survey of holiday camps was carried out, and committees for the selection of children were established in the four largest cities; a central committee for this purpose was constituted at the Hague.

Research was done by Professor Scheltema and Professor Gorter in 1924, 1925 and 1926. A committee of the health council was set up in 1925. In 1929 the state medical inspectors drew up a list of pros and cons, with reasons, if any, for temporary postponement, and this allowed the responsible doctor to improve his diagnosis and to give his findings on a special chart.

One must distinguish between treatment at the seaside and that in the woods, and between that in summer and that in winter. The latter is of importance financially and in connection with increased state subsides; its significance and extent have greatly increased in recent years.

More than half the children (boys 55 per cent and girls 65 per cent) sent out are in poor health. It must be observed that nervous children (boys 18 per cent and girls 8 per cent) are better off in the woods, whereas children with rickets, asthma and surgical tuberculosis should be sent to the seaside. As a rule sea air agrees with delicate children. The effect of the North Sea climate in the Netherlands tallies with the description by Haeberlin, Baudoin and Delcourt regarding the Belgian climate. Children may be sent to camp at any age from 5 to 15 years; there are also resorts for toddlers under 5, and recently camps have been started especially for the feebleminded and physically defective.

Life in the camps is governed by (1) exercise of various kinds (walking, games and gymnastics, led by experts if possible); (2) nourishing food and rest (rest halls, dormitories). It has been found necessary to train special nurses. Such training has been given since 1932 with official support.

Results obtained during residence are satisfactory. Attention is paid to increase in height and weight, general improvement of health, increase of percentage of blood corpuscles, increase of muscular power and local deviations. For a number of children a second period is desirable. An additional period of residence is necessary for many, as is shown by medical examination three months after their return home.

The value of the social and medical work done in these health camps is universally appreciated and is a contribution to the object in view: *Principiis obsta!*

AMESSE, Denver.

THE ORGANIZATION OF THE BATTLE AGAINST DISEASES DUE TO INTESTINAL PARASITES AMONG THE POPULATION OF U. S. S. R. K. S. SCRIABINE, Progrès méd., Sept. 12, 1936, p. 1417.

This is a rather long article describing first the recognition of the importance of a variety of intestinal worms and stressing the ease with which infection spreads when there is no medical supervision. In combating this spread and in curing those already subject to helminthiasis, central stations have been established throughout Russia. Instruction is given in individual care to prevent spreading and reinfection, and strict sanitary supervision is being instituted. LESLIE, Evanston, Ill.

A DISCUSSION OF "ANEUTROPHIA." PEDRO DE ALCANTARA, J. de pediat., Rio de Janeiro **2**:389 (Oct.) 1935.

This is a chapter from Dr. Alcantara's book entitled "An Introduction to the Physiology of Nutrition in Infancy." He has coined the word aneutrophia as being the exact opposite of neutrophia, which means a normal state. The physiologic processes of the child with aneutrophia are the opposite of normal, and this should be recognized, so that he will be treated accordingly.

SANFORD, Chicago.

CAUSES OF EARLY MORTALITY. OTTO SAXL, Monatschr. f. Kinderh. **64**:136 (Dec.) 1935.

In Prague the mortality among young infants decreased steadily from 1925 to 1932. From that time on there has been a slight increase. This curve parallels that for the general mortality. The general mortality and the early mortality of infants as well as the number of stillborn infants depend on social factors. The number of stillborn infants increases in proportion to the size of the community up to cities of 100,000, after which it begins to sink. The medical factors affecting stillbirth are debility, injury at birth, syphilis, obstetric operations and asphyxia.

When stillborn infants and those who die during the first month are included, debility heads the list of etiologic factors. Then follow asphyxia, injury at birth, syphilis and obstetric operations.

GERSTLEY, Chicago.

Prematurity and Congenital Deformities

FOETAL DEATH. C. A. C. LEGGETT, M. J. Australia **1**:288 (Feb. 29) 1936.

Leggett reviews the causes of antenatal and neonatal death and concludes that the most promising lines of attack in reducing neonatal mortality are those directed to complications of labor, syphilis and toxemias of pregnancy

TENNEY, Madison, Wis.

IMPERFORATE ANUS WITH URETERORECTAL FISTULA. E. CABANES, Nourrisson **24**: 158 (May) 1936.

A case is described in which an anal opening was established in the perineum by operation; the fistula was still present when the baby was 10 months of age.

MCCLELLAND, Cleveland.

PTERYGIUM COLLI CONGENITUM ET ELEPHANTIASIS CONGENITA. V. RANTASALO, Acta pædiat. **18**:368, 1936.

A 9 month old infant exhibited multiple congenital anomalies. Of these, the most conspicuous were bilateral folds of the skin of the neck, which extended

from the mastoid process to the acromion, and pitting edema of both lower extremities, more marked distally than proximally. In addition, there was a defect of the development of hair over both parietal regions; the right ear was larger than the left; the liver and spleen were enlarged. Both parents were healthy; no history could be obtained of the occurrence of similar deformities in other members of the family.

The classification and causes of such anomalies are discussed, and a brief but useful bibliography is appended.

McCune, New York.

A Case of Congenital Hemihypertrophy. J. Wallin, Acta pædiat. **18**:503, 1936.

At birth the left side of the infant's body was larger than the right; the asymmetry was particularly conspicuous in the extremities. Slight bluish discoloration was present about the left shoulder. The condition remained essentially unaltered during the period of observation, which extended through the fifth year of life. Biopsy of the skin and subcutaneous tissue of the left arm at 10 months of age prompted a histologic diagnosis of lymphangioma. Roentgen therapy was found to be ineffectual. Following an unsuccessful attempt at plastic repair of the left hand, sudden accumulation of fluid necessitated paracentesis of the skin in order to prevent the wound from breaking open. The fluid which was obtained was blood tinged and serous. The protein concentration was not determined. At 5 years of age the tissues of the left side of the body were swollen, firm and tense; the superficial veins were prominent. Roentgenographic examination revealed that the maturation of the skeleton had occurred in a symmetrical manner.

Aschoff recognizes two types of congenital hypertrophy: The first is local gigantism in which all parts of the affected region are involved proportionately; the second is congenital elephantiasis, which consists of unequal overgrowth of certain structures of the enlarged member. The most common varieties are: elephantiasis fibrosa, lipomatosa, angiomatosa, lymphangiomatosa and neuromatosa. It is customary to differentiate this condition from congenital lymphangiectatic edema and congenital elephantiasis as well as hereditary elephantiasis, or Milroy's disease. Certain forms occur in which the pathologic fractures are complicated by the presence of diffuse or localized changes of the subcutaneous connective tissue, telangiectases, nevi, lymphangiectasis and lymph cysts. Elephantiasis may be produced by the stasis which results from amniotic adhesions. The prognosis for the various types is different. The case reported here fits best into the category of congenital elephantiasis. There is a useful bibliography.

McCune, New York.

New-Born

Resuscitation of the New-Born. J. F. McGrath and K. Kuder, J. A. M. A. **106**:885 (March 14) 1936.

Many babies are believed to have been lost because of the lack of adequate treatment of asphyxia neonatorum. Many institutions have no standardized method of treating this condition, and even modern textbooks describe many measures formerly in use which are now untenable in competent practice. The authors advocate intubation by direct exposure and intratracheal insufflation of 10 per cent carbon dioxide and 90 per cent oxygen under measured pressure—a method developed by Flagg.

Bonar, Salt Lake City.

Obstetric Injuries to the Arms. P. Muller, Nourrisson **24**:154 (May) 1936.

Under this title are described fractures of the clavicle and humerus and brachial palsies occurring in 13,451 deliveries extending over a period of ten years. Fracture of the clavicle was observed only three times, fracture of the humerus six times and obstetric paralysis only twice.

McClelland, Cleveland.

ICTERUS NEONATORUM GRAVIS. F. THOENES, Monatschr. f. Kinderh. **65**:225 (April) 1936.

Thoenes reports three cases of icterus neonatorum gravis in one family. He made the diagnoses clinically and uses the cases to show that none of the classic signs, such as erythroblastosis, changes in the blood picture, large liver and spleen, petechiae and even biliuria, are infallible. He believes the condition can exist without true kernicterus and presents some evidence that the disease is transmitted through the father.

GERSTLEY, Chicago.

ON THE BIRTH OF ABNORMALLY BIG CHILDREN. T. KERN, Acta obst. et gynec. Scandinav. **16**:189, 1936.

A study of the puerperium in 228 deliveries in which the birth weight of each infant exceeded 4,500 Gm. (0.92 per cent of 24,644 births) discloses that pregnancy was protracted in 52.6 per cent, that a preponderance of the infants were boys (67.5 per cent) and that increased fetal weights were associated with multiparity, increase in age and higher than average weight in the mother.

Operative intervention during delivery was necessary in 19.3 per cent; hemorrhage of more than 500 cc. occurred in 24.1 per cent (normal 4.9 per cent).

The death rate among the children was 14.9 per cent.

Prophylaxis consists in inducing parturition when the fetus has attained a normal birth weight.

ADAIR and POTTER, Chicago.

ETIOLOGIC FACTORS IN NEONATAL MORTALITY, WITH SPECIAL REFERENCE TO CEREBRAL HEMORRHAGE. K. U. TOVERUD, Acta pædiat. **18**:249, 1936.

Statistics from many countries support the generalization that from 50 to 60 per cent of all infants who die during the first year of life succumb within the first thirty days after birth. In order to effect further reduction of the death rate among infants under 1 year of age it will be necessary to concentrate attention and effort on this fateful month.

During the decennium between 1924 and 1933, autopsies were performed in the department of pathology of the University of Norway on 953 newly born infants. Of these, 534 were born prematurely and 419 at term; 587 were born dead and 366 alive. The causes of death when determinable were as follows: cerebral hemorrhage, 38.8 per cent; congenital malformations, 5.1 per cent; congenital syphilis, 1.3 per cent; pneumonia, 1.6 per cent. Other causes, such as melena neonatorum, adrenal hemorrhage, subcapsular hemorrhage of the liver, hemothorax, sepsis, peritonitis and ileus, considered individually, represented less than 1 per cent of the fatalities. In 51.4 per cent of the cases the pathologic observations did not account for death, although scattered subserous hemorrhages were frequently present.

The importance of intracranial and intraspinal hemorrhage in newly born infants is being accorded increasing attention; such hemorrhages are usually ascribed to mechanical causes or to alterations in the coagulability of the blood. In the present series 57.3 per cent of the patients who exhibited bleeding which affected the central nervous system were premature infants; in the majority of the cases delivery had not been difficult, prolonged or precipitate; in 2.7 per cent of the cases the infant had been born by cesarean section. Furthermore, the observation was made that about 80 per cent of the mothers of infants who had hemorrhage exhibited some sort of pathologic complication of pregnancy. In 10 of 56 autopsies which Toverud scrutinized with especial care there was evidence to indicate that the bleeding had occurred before delivery began; in a number of these cases ecchymoses were present in the tooth buds. Histologically these hemorrhages resembled those found in scurvy. In 7 cases of hemorrhage in the tooth buds the concentration of vitamin C in the liver was so low as to indicate the presence of latent scurvy.

The importance of physical trauma in producing hemorrhage in the newly born infant cannot be denied; however, the health of the mother as it affects the physical integrity of the fetus must be given due consideration.

McCUNE, New York.

ERYTHROBLASTOSIS NEONATORUM TEMPORARIA; CONGENITAL ERYTHROBLASTOSIS WITHOUT HYDROPS, ICTERUS OR ANEMIA. L. SALOMONSEN, Acta pædiat. **18**:357, 1936.

There is a growing tendency to classify congenital hydrops, icterus gravis neonatorum and congenital anemia of the newly born in the same etiologic category and to regard them as different manifestations of the same fetal morbid entity. Concerning the cause little is known. Aspects of the disease which are of greater fundamental import than the foregoing triad are: erythroblastosis, erythroleukoblastosis, splenomegaly, active extramedullary hematopoiesis and hyperplasia of the bone marrow. One of the most cogent reasons for believing that congenital hydrops, icterus gravis and congenital anemia are in some way or other closely related is that they have been observed to occur serially, although in varying sequence, in successive infants born of the same mother. According to von Gierke, the common feature of all cases is erythroleukoblastosis, which is defined as the presence of embryonal blood cells in the peripheral circulation. If this concept is true, one might expect to encounter examples of the disease in which erythroblastosis would be the sole or predominating manifestation.

Salomonsen realized this expectation. He reports the cases of two newly born infants who exhibited thick, puffy skin, conspicuous enlargement of the liver and marked erythroblastosis during the first few days of life. In one case the spleen was greatly enlarged; in the other there was transient jaundice. In neither case was anemia present. The mother of one patient had suffered two miscarriages and had been delivered of one macerated fetus. Both children survived, the one after a small transfusion, the other without treatment. Although no identical cases have been published, one of the members of a family reported by de Lange as showing icterus gravis manifested significant but transient erythroblastosis.

Salomonsen expresses agreement with Lehndorff that general edema is to be regarded as a more severe expression of the operation of the same cause which when it affects the fetus later or less intensely produces icterus gravis or congenital anemia. Arguments are drawn by analogy from a form of transmissible erythroblastosis which occurs in chickens. McCUNE, New York.

ANEMIA NEONATORUM. BENT ANDERSEN, Hospitalstid. **79**:657 (June 16) 1936.

Andersen describes in detail a case of anemia neonatorum (primary anemia of the new-born). He discusses the possible relationship of this condition to congenital hydrops and icterus gravis, pointing out that the etiology and pathogenesis still are not well understood. ELGHAMMER, Chicago.

Acute Contagious Diseases

CAUSES OF DEATH IN DIPHTHERIA AND THEIR PREVENTION. A. L. HOYNE, Am. J. M. Sc. **191**:271 (Feb.) 1936.

When the diphtheria membrane is located within or below the larynx, diphtheria antitoxin alone will seldom save the patient. Usually intubation or tracheotomy is required. Although there is no absolute method for preventing bronchopneumonia in diphtheria, the frequency of this complication can be held to a minimum if minute attention is paid to maintaining the cleanliness of the hands and instruments when performing intubations, and if correct methods of feeding are followed for patients wearing intubation tubes. Diphtheritic myo-

carditis can often be prevented by the use of a 10 per cent solution of dextrose intravenously, provided this treatment is begun sufficiently early and continued daily for a sufficient length of time.

The causes of death from diphtheria fall into three classes: (1) asphyxia, (2) bronchopneumonia and (3) myocarditis (toxemia). HENSKE, Omaha.

ENCEPHALOMYELITIS FOLLOWING GERMAN MEASLES. H. HOUSTON MERRITT and YALE D. KOSKOFF, Am. J. M. Sc. **191**:690 (May) 1936.

Four cases of encephalomyelitis following rubella are reported, and the literature pertaining to this subject is reviewed. A table of data of seven previously reported cases and of these four is presented, covering signs and symptoms. These cases are compared with those occurring after measles (morbilli).

HENSKE, Omaha.

A FIFTH YEAR'S OBSERVATION ON MALARIA IN PANAMA, WITH REFERENCE TO THE FAILURE OF ATABRINE TO CONTROL THE EPIDEMIC. W. H. KOMP and H. C. CLARK, Am. J. Trop. Med. **16**:109 (March) 1936.

Komp and Clark review their work during the fifth year of a study of malaria in Panama. They were unable, by employing various methods in which quinine, atabrine and plasmochin were used, to check or prevent the development of epidemics of malaria.

They state that their experience with malaria in Panama has caused them to abandon the methods used in the past, the attempts to reduce the incidence of malaria by treatment directed against malaria in children and adolescent patients. They believe that this has done more harm than good, as it tends to disturb or destroy the natural immunity that may be built up by repeated infections in childhood. In all the clinical cases, however, the patient is actively treated.

BURPEE, Augusta, Ga.

CLINICAL ASPECTS OF POLIOMYELITIS. HARRY LOWENBURG, Arch. Pediat. **52**: 721 (Nov.) 1935.

This review of the well known facts concerning the symptoms, diagnosis and treatment of poliomyelitis is not abstracted. WADDELL JR., University, Va.

EPIDEMIC MENINGOCOCCUS MENINGITIS: AN ANALYSIS OF TWENTY-SIX CASES, TWENTY-ONE OF WHICH OCCURRED IN THE SPRING OF 1935. WILLIAM S. TILLETT and THOMAS MCPHERSON BROWN, Bull. Johns Hopkins Hosp. **57**:297 (Nov.) 1935.

The number of cases is small. There appeared to be three well defined types of onset: (1) mild infection of the upper respiratory tract of from one to three weeks' duration before evidence of meningitis appeared. (2) Onset initiated by symptoms referable to the upper respiratory tract, but differing from the first type in that it was more severe and the time between the first symptoms and the meningitis was only a few days. (3) Sudden and sometimes explosive onset, with symptoms directly and primarily referable to meningitis but with no history of any preceding infection in the nose or throat.

Among extrameningeal complications epididymitis occurred in two patients (0.9 per cent).

Early in the treatment serum was administered both intravenously and intraspinally at six hour intervals. Later in the course treatment was determined by the condition of the patient and by laboratory examination. Only one of the patients died, but the series is too small to justify any conclusions as to the treatment.

LYTTLE, New York.

THE EXPERIMENTAL PRODUCTION OF WHOOPING COUGH IN CHIMPANZEES. ARNOLD R. RICH, PERRIN H. LONG, J. HOWARD BROWN, ELEANOR A. BLISS and L. EMMETT HOLT JR., Bull. Johns Hopkins Hosp. **58**:286 (April) 1936.

Because of the unsatisfactory results of inoculation of animals with cultures of the Bordet-Gengou bacillus and because anatomic changes found in patients with pertussis suggest virus disease, the authors do not regard Koch's postulates as having been satisfactorily fulfilled in relation to the Bordet-Gengou bacillus and pertussis.

They undertook experiments to test the hypothesis that pertussis might belong in the group of diseases with a dual etiology, such as hog cholera (caused by a filtrable virus associated with Bacterium suipestifer) and canine distemper (due to a filtrable virus associated with Bacterium bronchisepticum).

Their conclusions are as follows:

1. A condition similar in all respects to whooping cough and characterized by coryza followed by a protracted paroxysmal cough typical of that of pertussis, associated with lymphocytosis and the development of a positive complement fixation reaction for the Bordet-Gengou bacillus, has been produced in the chimpanzee by oral inoculation of unfiltered exudate from the tracheas of human beings with pertussis. The Bordet-Gengou bacillus was recovered on cough plates at the height of the cough.

2. A precisely similar condition has been produced in the chimpanzee by oral inoculation of pure cultures of the Bordet-Gengou bacillus. It is therefore clear that the characteristic clinical features of pertussis can be produced in apes by these bacilli acting alone.

3. The inoculation of apes with bacteriologically sterile blood and filtered secretions of the respiratory tract obtained from each of four patients with pertussis early in the disease was followed by the appearance of catarrh of the upper respiratory tract, without cough. In the one instance in which an attempt was made to transfer the agent from one ape to another by means of a bacteriologically sterile filtrate of the nasopharyngeal secretions the attempt was successful.

4. The nature of this filtrable agent is discussed. Its relation to pertussis is undetermined. At present one can say only that the Bordet-Gengou bacillus, acting alone, is capable of producing the characteristic clinical manifestations of whooping cough in the ape.

LYTTLE, New York.

POLIOMYELITIS—THE LOS ANGELES EPIDEMIC OF 1934. R. W. MEALS, V. F. HAUSER and A. G. BOWER, California & West. Med. **43**: 123 (Aug.); 215 (Sept.) 1935.

A valuable analysis is made of about 1.800 cases of poliomyelitis in Los Angeles and the vicinity. The authors believe that a different strain of virus was the causative agent, because of the atypical clinical picture, the high incidence of the disease in adults, especially among doctors and nurses (37 per cent of the patients were 15 years of age or over), the appearance of mild symptoms in a few patients who had previously had poliomyelitis and the failure of convalescent serum to alter the course of the disease in some cases of fatal outcome occurring early in the epidemic.

In 11 cases of the bulbar type the outcome was fatal, and pathologic examination showed microscopic changes characteristic of poliomyelitis.

The symptoms were variable, ranging from severe headache, with abdominal cramps, diarrhea and vomiting, to neuralgic signs with no premonitory symptoms. The most constant symptom was pain on flexion of the spine, which was often present with no stiffness of the neck or spine. The signs were also variable. Acute muscular tenderness and hyperesthesia were frequent. Often marked fatigability was the only sign elicited in the examination of an affected part. Signs of involvement of the sympathetic nervous system were prominent, such as abdominal pain,

distention and vomiting, without rigidity, retention of urine or localized pain and sweating over the affected extremities.

Convalescence was rapid and complete in most cases. In several instances of the mild form relapse after apparent recovery was observed.

In 20 per cent of the series residual paralysis or paresis was shown. A series of remote sequelae were observed, occurring more frequently than has previously been noted. Insomnia, nightmare, emotional instability, mental fatigability and lack of power of concentration were often met. Neurocirculatory asthenia, localized, recurrent edema and trophic disturbances indicated sympathetic nervous and vasomotor instability.

A series of cases in which the history simulated that of poliomyelitis are cited, including instances of infectious transverse myelitis, intracranial tumor, hemangioma and tumor of the spinal cord, as well as malaria, typhoid and puerperal sepsis.

The use of convalescent serum as a prophylactic measure proved ineffective. In 23 per cent of 207 doctors, nurses and hospital attendants so treated, the disease developed within three weeks of the treatment.

The authors believe that convalescent serum given intravenously and intramuscularly has definite value in the early treatment of the disease.

MARSHALL, San Francisco.

EYE COMPLICATIONS OF THE ACUTE EXANTHEMATA IN CHILDREN. RICHARD C. GAMBLE, Illinois M. J. **69**:229 (March) 1936.

In this article Gamble cites the various ocular complications of the acute exanthems. He divides them into two groups: the common ones, which occur early, such as the various types of inflammation of the lids, conjunctiva and cornea caused by the specific cutaneous eruptions involving these structures, and the less common ones, which occur later in the diseases—the inflammations of the intra-ocular structures, of the orbit and of the optic nerve. The latter are more serious, and the diagnosis may be much more difficult in such cases.

BARBOUR, Peoria, Ill.

ACTIVE IMMUNIZATION AGAINST POLIOMYELITIS. M. BRODIE and W. H. PARK, J. A. M. A. **105**: 1089 (Oct. 5) 1935.

Controlled clinical and experimental studies have shown that convalescent serum is not efficacious in the treatment of the preparalytic stage of poliomyelitis. Epidemiological evidence suggests that immunity to the disease develops with aging and is the result probably of exposure to the virus. Since with natural immunization some persons contract the disease, a safe, effective method of artificial immunization is preferable, that is, the use of a vaccine which is antigenic, safe and innocuous. This report deals with the use of such a vaccine in the immunization of monkeys and man and with tests to determine the degree of this immunity. The selected preparation was the virus inactivated by germicides, of which a solution of formaldehyde was found to be the best. In animals a dose of 5 cc. was sufficiently antigenic to produce an immunity better than that developed after a mild attack of the disease and sometimes comparable to that produced by a severe attack or by immunization with the active virus. The vaccine was found to be noninfective, not only in animals but in man. In 2,300 vaccinations of children only 3 general reactions and 23 local reactions occurred. Seventy-five children were tested for antibodies both before and after immunization. The antibody response seemed to be best in children that were the most susceptible. Although the vaccine produces an antibody response in children which compares favorably with that developed after the disease, the test of its value must await studies during epidemics. The antibody becomes apparent in one week and reaches its full development in from three to four weeks. It has been demonstrated eight months afterward. The material appears to be safe, as demonstrated in the immunization of monkeys and 2,300 children.

BONAR, Salt Lake City.

SCARLET FEVER IMMUNIZATION DURING A SCHOOL EPIDEMIC. H. S. DIEHL and R. G. HINCKLEY, J. A. M. A. **106**:1354 (April 18) 1936.

In an attempt to control an epidemic of scarlet fever among 436 students, active and passive immunization was utilized. The number of new cases declined promptly after the third dose of scarlet fever toxin. A large proportion of the patients manifested a mild reaction, and about 5 per cent were admitted to the infirmary after each injection. The reactions were mild and of short duration. A rash was present in some cases. Antitoxin was given to 25 exposed susceptible persons; 76 per cent had slight, and 68 per cent moderate or severe, serum reactions. The disease developed in 5 of this group. BONAR, Salt Lake City.

CONTROL OF MENINGOCOCCIC MENINGITIS EPIDEMICS. D. M. KUHNS, J. A. M. A. **107**:5 (July 4) 1936.

The usual methods of control failed in an epidemic of meningococcic meningitis. An attempt was made to determine the reactivity of the skin in the presence of Gordon's four types of meningococcus by using the filtrable separable fractions of meningococcus broth cultures. The filtrate was tried in an epidemic to determine its value as a skin-testing and as an immunizing substance. Skin testing on sensitive and susceptible persons appears to be the best means of determining the toxicity of the exotoxin. Immunization of 395 persons with the full strength filtrate was performed. At the end of ten months none had contracted meningococcic meningitis, although in the C.C.C. Camp where the immunization was carried out four persons who were not so treated acquired the disease.

BONAR, Salt Lake City.

SENSITIVITY TO B. DYSENTERIAE. B. G. EFRON and D. N. SILVERMAN, J. Allergy **7**:145 (April) 1936.

The authors' summary is as follows:

"Sensitivity to B. dysenteriae occurs in sporadic cases of infection with this organism. The sensitivity, while showing a distinct tendency to be specific for the individual strain with which the patient is in contact, is, however, apparently group specific in that reactions occur to other strains of the organism with which the patient is not in contact.

"We have not as yet determined the incidence of sensitivity in these sporadic cases of bacillary infection."

HOYER, Cincinnati.

CHANGES IN MORPHOLOGY OF HEMOPHILUS PERTUSSIS GROWN UNDER VARYING CONDITIONS AND ON DIFFERENT MEDIUMS. JOHN A. TOOMEY and WILLIAM S. TAKACS, J. Bact. **31**:44 (Jan.) 1936.

Toomey and Takacs observed that freshly isolated cultures of Haemophilus pertussis grown on blood agar containing from 20 to 25 per cent hemoglobin (Bordet's medium) at p_H 6 appear as small ovoid bacilli, at times nearly indistinguishable from coccoid bacteria. When these organisms are transferred every four days on the same medium they begin to elongate after from 160 to 180 transplant generations, while their virulence and antigenic activity remain the same or are slightly diminished. The organisms acquire a new quality, that of adhesiveness, not seen in freshly isolated cultures. A single passage through a guinea-pig brings the organism back to its original ovoid form. It likewise regains what little virulence it has lost and loses its tendency to stick to the medium.

The authors also noted that organisms adapted to veal brain agar medium at p_H 7.8 elongate from five to ten times the length of the original bacillus isolated on blood agar medium as soon as they begin to grow luxuriantly. This occurs approximately 10 transfer generations removed from the parent strain, at which time the organisms become relatively less virulent and less antigenic. When long

bacillary organisms adapted to veal brain agar at p_H 7.8 are readapted (140 generations of retransplanting) to hemoglobin blood agar medium having a gradually decreasing p_H they diminish in size and in length. STOESSER, Minneapolis.

TESTS FOR IMMUNITY TO ACUTE ANTERIOR POLIOMYELITIS. J. A. KOLMER and A. M. RULE, J. Immunol. **29**:175, 191 and 199 (Sept.) 1935.

Kolmer and his associates, in a series of three papers, report the results of their experience with various methods for testing immunity to acute anterior poliomyelitis. Normal monkeys, normal adults and normal children show no reaction of the skin which could be ascribed to the virus after the intracutaneous injection of an emulsion of the spinal cord of a monkey with poliomyelitis. Cutaneous tests, therefore, are of no value as indicating immunity.

Colloidal gold, complement fixation and precipitation tests on the serum could not be reliably employed to determine immunity to poliomyelitis.

The monkey serum neutralization test is the only reliable test for immunity. The authors describe their standard technic for this test.

FOTHERGILL, Boston.

EFFECT OF GONADOTROPIC AND OESTROGENIC HORMONES ON AGGLUTININ RESPONSE TO B. PERTUSSIS IN IMMATURE ANIMALS. J. H. DINGLE, R. K. MEYER and E. L. GUSTUS, J. Immunol. **30**:139 (Feb.) 1936.

It was shown that the agglutinin response of rats and rabbits immunized with Bacillus typhosus and Bacillus pertussis vaccines varied with the sexual maturity of these animals. Poor responses were obtained in young immature animals. The agglutinin response was then followed in young animals treated with various sex hormones, namely, gonadotropic hormone obtained from pregnant mare serum, gonadotropic substance from the urine of pregnant women, theelin and pituitary implants. This group did not exhibit a significantly greater response than the controls, although there was a definite increase in the development of the gonads.

FOTHERGILL, Boston.

PROTECTIVE MEASURES IN DIPHTHERIA INTOXICATION. P. J. HANZLIK and B. TERADA, J. Pharmacol. & Exper. Therap. **56**:269 (March) 1936.

In pigeons poisoned with diphtheria toxin Hanzlik and Terada investigated the effects of remedies that others have found beneficial in diphtheria or dysentery poisoning of animals: digitalis, sodium sulfocyanate (dysentery), cevitamic acid and the untried congo red (as a colloidal adsorbent for diphtheria toxin). Cevitamic acid acted as hydrochloric acid with a similar p_H, giving the same results. For practical purposes all the remedies, except cevitamic acid, when previously mixed with diphtheria toxin were ineffective. Pigeons were used because they respond typically to diphtheria toxin and digitalis.

PILCHER, Cleveland.

ADJUSTMENTS DURING FOUR YEARS OF PATIENTS HANDICAPPED BY POLIOMYELITIS. ELLEN H. BARBOUR, New England J. Med. **213**:563 (Sept. 19) 1935.

This study was made with the purpose of determining the physical improvement and the emotional adjustment, during a period of four years, of sixty children who were victims of infantile paralysis. In 1930 the degree of paralysis of these children was described in social terminology. Briefly, the patients were classified under the following heads: educationally handicapped so that the patient's educational progress was definitely impeded; occupationally crippled, the paralysis prohibiting the patient from certain occupations in later life, and socially handicapped, with disfiguring paralysis which might be a source of social embarrassment.

In 1930 over one half of all the children were in the socially handicapped group; approximately one fourth were in the most severely crippled, educationally impeded group, and a little less than one fifth were described as occupationally handicapped. In the 1934 redistribution the paralysis of one half of the children in the total group had disappeared, and in one half of the children who were still crippled only the mildest degree of paralysis remained. In slightly more than one child in five, the paralysis was an occupational handicap, and only one in fifty was severely limited in motion. In the occupationally handicapped group the least change was shown, and the marked decrease in the number of the socially handicapped children seems to indicate that such a child has an excellent chance of being normal at the end of four years of treatment.

The scholastic retardation was an interesting social factor in this study. Twenty-five of forty children were not educationally retarded at the end of four years; nine were retarded one year; four were retarded two years, and two were retarded three years. Six of the twenty children who are still paralyzed are emotionally maladjusted to their handicap.

GENGENBACH, Denver.

WHOOPING COUGH AND ITS PREVENTION. LOUIS SAUER, New England J. Med. **213**:1061 (Nov. 28) 1935.

Carriers, patients with second attacks and patients suspected of having whooping cough who never whoop, in all of whom the condition would otherwise remain undetected, may have their condition diagnosed bacteriologically. The earlier cough plates are exposed the more likely will they be found positive. Negative findings do not exclude the disease.

The culture medium is always made with human blood. The vaccine contains no alien protein, formaldehyde or other denaturing agent. It is refrigerated until used. Each 1 cc. of the vaccine contains 10,000,000,000 bacilli. Since 1931 the vaccine has been injected as follows: One cubic centimeter is injected just under the skin in the deltoid region of each arm; one week later 1.5 cc. is injected in the region of the biceps muscle of each arm; one week thereafter 1.5 cc. is injected in the region of the triceps muscle of each arm. When the vaccine is properly administered, no untoward effect should occur.

The average age of the 1,609 children at the time of injection was about 11 months. The best age for immunization against pertussis is between the seventh and twelfth months of life. Ninety per cent of the children given the injections did not contract pertussis when exposed.

The following schedule of immunization, used for several years, has been found practical: Immunize first against whooping cough (at from 7 to 12 months); four months later immunize against diphtheria (with toxoid or alum toxoid). When the Schick test is performed and found negative, vaccination against smallpox is performed; immunization against scarlet fever may be completed before attendance at nursery school or kindergarten.

GENGENBACH, Denver.

ACTIVE IMMUNIZATION AGAINST POLIOMYELITIS. MAURICE BRODIE, New York State J. Med. **35**:815 (Aug. 15) 1935.

Isolation of persons who have been in contact with patients suffering from poliomyelitis is of little value in preventing poliomyelitis because of the high proportion of carriers. Serum therapy is of no value as the disease is confined to the central nervous system. Only 12 second attacks in human beings have been reported, suggesting that there is only one strain of virus. Virus inactivated with solution of formaldehyde, U. S. P., is perfectly safe; no harmful effects were noted in 3,000 inoculations, and but few general reactions developed. Two doses of the vaccine stimulated the production of antibodies in practically all persons treated. It takes about one week for protection to develop, and with two doses it is present after eight months. Whether the protection afforded is sufficient remains to be seen.

AIKMAN, Rochester, N. Y.

THE PREVENTION OF POLIOMYELITIS. WILLIAM H. PARK, New York State J. Med. **35**:818 (Aug. 15) 1935.

Although Park feels that the experiences of his own department show little if any therapeutic value of convalescent serum, his mind is still open and he expresses the belief that further investigation should be carried on. Without a test for susceptibility general immunization with vaccine would present a tremendous problem. At present immunization should probably be advised only when epidemics threaten.

AIKMAN, Rochester, N. Y.

CLINICAL MANAGEMENT OF POLIOMYELITIS. E. B. SHAW, Northwest Med. **35**:39 (Feb.) 1936.

This is a general article in which the pathologic changes, symptoms, diagnosis and treatment of poliomyelitis are considered. Shaw observed no damage to the lungs as did Landon. He believes that the clinician should continue to use convalescent serum until a better method of treatment appears. He believes in giving from 50 to 100 cc. of serum intramuscularly every twelve to twenty-four hours during the preparalytic stage. He likewise recommends transfusion. He believes that prophylactics containing attenuated virus are not without danger.

SCOTT, Philadelphia.

EPIDEMIC MENINGITIS: TREATED BY INTRAVENOUS INJECTIONS OF MENINGOCOCCUS ANTITOXIN. JACK R. KAREL, Northwest Med. **35**:48 (Feb.) 1936.

A man aged 44 had the usual signs and symptoms of meningitis. The spinal fluid cell count was 37,600, and a meningococcus was recovered. The record of treatment follows:

On the first day the white cell count of the blood was 37,600. Meningococcus antitoxin given in a dose of 60 cc., or 20,000 units, and 120 cc. of a 10 per cent solution of dextrose was given intravenously.

On the second day the cell count was 22,050. The same dose and dextrose were given.

On the third day the cell count was 7,940. The same dose and dextrose were given.

On the fourth day the cell count was 10,750. The same dose was given.

On the fifth day the cell count of the spinal fluid was 1,334. A smear gave negative results; a culture showed positive findings.

On the seventh day 30,000 units of antitoxin was given intravenously.

On the eighth day 20,000 units of antitoxin was given intravenously.

On the twelfth day the cell count of the spinal fluid was 45. Cultures did not reveal any organisms.

On the sixteenth day the patient was discharged from the hospital.

The total amount of serum given was 390 cc., or 130,000 units. There was no serum reaction.

SCOTT, Philadelphia.

MODERN METHODS OF PREVENTING MEASLES. J. S. BAIRD and L. W. PUMPHREY, Pennsylvania M. J. **39**:765 (July) 1936.

In sixty-six children (average age, 4 years) the prevention of measles with placental extract was attempted. In 58 per cent measles was successfully prevented. In the remaining 42 per cent, generally speaking, the attack was modified —with an average incubation period of eighteen days. The striking feature of the study, however, appears to be in the 100 per cent prevention attained in fourteen children with whole (unfractionated) placental extract. Obviously, fractionation is desirable if it is possible, in the interest of refinement and concentration of the material, but in the group treated with the several different protein fractions only 46 per cent were fully protected. This appears to agree with McKhann's observation that the fractional preparations, i. e., those containing only euglobulins or pseudoglobulins, do not have the same measles antibody potency as the whole extract. It is hoped that a method will be speedily found by which the antibody potency of the whole placental bulk will be made available. It is this material which, as shown, gave perfect prevention.

LOGUE, Williamsport, Pa.

REPORTING PARALYTIC AND NONPARALYTIC POLIOMYELITIS. Pub. Health Rep. **51**: 43 (Jan. 10) 1936.

In all reports made in the future by the department of public health of Massachusetts, the condition will be classified as paralytic or nonparalytic. This action is taken in order to obtain a true picture of the current prevalence of the disease. In former years cases of the nonparalytic form were not reported as frequently as they are at present.

SANFORD, Chicago.

PREVENTION OF INTRAVENOUSLY INOCULATED POLIOMYELITIS OF MONKEYS BY INTRANASAL INSTILLATION OF PICRIC ACID. CHARLES ARMSTRONG, Pub. Health Rep. **51**:241 (March 6) 1936.

Trinitrophenol instilled into the nostrils tends to protect monkeys from ill effects of intravenous injection of poliomyelitis virus. These results tend to confirm the conclusions of Lennette and Hudson, based on actual section of the olfactory tract, that intravenously injected poliomyelitis virus produces infection of the central nervous system by way of the nasal membranes and the olfactory tract.

SANFORD, Chicago.

SUMMARY OF CURRENT PREVALENCE OF COMMUNICABLE DISEASES IN THE UNITED STATES. Pub. Health Rep. **51**:263 (March 13) 1936.

For the period of Jan. 26 to Feb. 22, 1936, meningococcic meningitis increased in all the areas except the south-central. The current incidence was the highest since 1931. Influenza also showed an increase, 28,549 cases having been reported. This is only 80 per cent of the incidence for the same period of 1935. The incidence of smallpox, which was at the highest level in recent years, declined somewhat. Scarlet fever, with 29,134 cases, showed the highest incidence in recent years. The incidence of diphtheria, typhoid, measles and poliomyelitis continued to be low. The mortality from all causes was 13.8 per thousand, the highest for this period since 1931.

SANFORD, Chicago.

HISTORY AND FREQUENCY OF SMALLPOX VACCINATIONS AND CASES IN 9,000 FAMILIES. S. D. COLLINS, Pub. Health Rep. **51**:443 (April 17) 1936.

The studies reported were made during a twelve month period from 1928 to 1931 in one hundred and thirty localities in eighteen states. The surveyed families were located in urban, rural and metropolitan areas. Only from 10 to 20 per cent of the children had been vaccinated before the age of entrance to school; from 85 to 90 per cent of the adults had been vaccinated within seven years. The vaccination rate was 31 per thousand persons of all ages and 49 per thousand persons under 20 years of age. Among the 17 cases of smallpox that occurred, 16 were those of persons who had never been vaccinated, a rate of 96 per hundred thousand, as compared with 1 case (the patient had been vaccinated forty years previously), or a rate of 5 per hundred thousand, among persons who had been vaccinated at any time.

SANFORD, Chicago.

CURRENT PREVALENCE OF COMMUNICABLE DISEASES IN THE UNITED STATES. Pub. Health Rep. **51**:871 (July 3) 1936.

Influenza, poliomyelitis, meningococcic meningitis, scarlet fever, diphtheria, typhoid and measles showed a seasonal drop for the period of May 17 to June 13, 1936. Smallpox showed the highest incidence since 1932. It was prevalent in the north-central, mountain and Pacific regions. The mortality from all causes was 11.4 per thousand of population. This is about the usual figure.

SANFORD, Chicago.

CURRENT PREVALENCE OF COMMUNICABLE DISEASES IN THE UNITED STATES, SEPT. 6 TO OCT. 3, 1936. Pub. Health Rep. **51**:1455 (Oct. 23) 1936.

For the period from Sept. 6 to Oct. 3, 1936, the number of cases of poliomyelitis rose to 1,027. States reporting increases were: Illinois, 245; Ohio, 102; Tennessee, 85; California, 54; Alabama and Georgia, 40 each, and Colorado, 29. For the country as a whole this incidence was about 40 per cent of that for the corresponding period last year. There was a seasonal increase in the number of cases of scarlet fever to 5,215 cases, while the incidence of influenza, typhoid, smallpox, measles and diphtheria remained low. The number of cases of meningococcic meningitis (237) was similar to that for 1935, but both figures are above that for the preceding three year period.

SANFORD, Chicago.

THE MANAGEMENT AND TREATMENT OF MENINGOCOCCUS MENINGITIS. GEORGE M. CULTRA, South. M. J. **28**:1136 (Dec.) 1935.

The author believes that successful treatment of meningococcic meningitis depends on early and vigorous treatment. An initial blood transfusion seems to raise the patient's resistance to infection and supplement serum therapy. Intravenous administration of serum in the early stages is indicated, for at that time bacteremia is present. The reactions are no greater than those with any other form of serum therapy. Repeated lumbar puncture may cause the cell count of the fluid to remain high. These cells are, however, lymphocytes and not polymorphonuclear leukocytes.

The injection of serum into the ventricles and into the cisterna gives excellent results in the hands of persons skilled in this technic, but it is not advocated as a routine measure in private practice unless symptoms of obstruction occur.

SCHLUTZ, Chicago.

THE POLIOMYELITIS EPIDEMIC IN NORTH CAROLINA. ALDERT S. ROOT, South. M. J. **29**:184 (Feb.) 1936.

The author reports experiences obtained from the North Carolina epidemic, which totaled 622 cases. Less than 10 per cent of the persons afflicted received hospital care. There were 12 instances of second attacks in the same family.

The Park-Brodie vaccine was given as a prophylactic agent to 300 children in several counties. In about 6 per cent of the 300 children who received the vaccine, abscess developed at the site of the intradermal injection, and in about 12 per cent rather large nodules. In a few children constitutional reactions followed vaccination. Both the systemic and the local reaction were worse after the second dose.

The attitude of the 25 members of the North Carolina Pediatric Society was one of skepticism, only 2 of the number having advocated the general use of the vaccine. The general impression prevailed that convalescent serum was of doubtful value. There is a general consensus that after the first symptom is evident and the virus has invaded the neurons neither injection of convalescent serum or pooled blood nor blood transfusion has any effect on the extent of the paralysis.

The number of injections of convalescent serum or pooled blood or of blood transfusions given in the North Carolina epidemic was small, and the authors prefer not to draw conclusions on this basis.

SCHLUTZ, Chicago.

CONGENITAL MALARIA. N. C. TANNER and R. E. L. HEWLETT, Lancet **2**:369 (Aug. 17) 1935.

This is a report of the occurrence of malaria in the second-born of dizygotic twins. The mother had malaria throughout the pregnancy. Parasites of tertian malaria were discovered in the patient's blood when the infant was admitted to the hospital at the age of 50 days. In the absence of a known placental trauma

or infarct, premature separation of the placenta was considered the most probable cause of the transmission of the infection. Treatment with iron and atabrine improved the anemia and cured the malaria. LANGMANN, New York.

TREATMENT OF ACUTE ANTERIOR POLIOMYELITIS IN THE EARLY STAGES. R. SOUTHBY, M. J. Australia **2**:367 (Sept. 21) 1935.

In the general treatment of poliomyelitis Southby believes that (1) moderate reduction of intracranial tension by lumbar puncture is most beneficial as regards both the immediate improvement of symptoms and the degree of subsequent paralysis, if any, and that (2) the employment of diathermy over the cervical or lumbar enlargement of the spinal cord, depending on the extremities involved, affords relief of hyperesthesia and muscular pains. In respect to convalescent serum he believes that (1) it is helpful in many cases, that (2) the route of administration makes little difference and, consequently, intramuscular injection, being the easiest, becomes the method of choice and that (3) convalescent serum has no value in checking a rapid spread of paralysis and, consequently, should not be given after paralysis has developed. GONCE, Madison, Wis.

THE EARLY TREATMENT OF POLIOMYELITIS. J. MACNAMARA, M. J. Australia **2**: 374 (Sept. 21) 1935.

Macnamara insists that the best protection against paralysis in the early stage of poliomyelitis is adequate injection of immune human serum. The serum must come from a donor who is frankly paralyzed as a result of an attack of undoubted poliomyelitis within the preceding five years. Reported failures in the effectiveness of the serum in the treatment of the disease are due to the use of serum obtained from normal adults and from persons who are paralyzed as a result of diseases other than poliomyelitis and to the use of potent serum in the so-called preparalytic stage, in which, however, unrecognized paralysis already is present at the time of injection of the serum. The serum must be potent and must be given in the preparalytic stage of the disease.

The serum should be given by the intravenous and perhaps by the intrathecal route. Intramuscular injection is easy, but "the injection of a serum by a route which requires many hours to elapse before the serum is absorbed is as futile a proceeding as a fireman attempting to extinguish a fire the day after the alarm is given." Depending on the potency of the serum and on the stage and severity of the disease, the effective intravenous dose varies from 70 to 250 cc.

The value of immune serum in the treatment of poliomyelitis does not need to be proved by statistical methods, with the omission of treatment in alternate cases. As in the use of antitoxin for diphtheria and of appendectomy for acute appendicitis, the value rests on the summation of clinical impressions rather than on statistical proof. GONCE, Madison, Wis.

USE OF MIXED VACCINES IN PREVENTION OF BRONCHOPNEUMONIA FOLLOWING MEASLES AND WHOOPING COUGH. F. CHEVREL, Nourrisson **24**:96 (March) 1936.

Statistics are offered to show that pulmonary complications after measles and whooping cough were greatly reduced by the prophylactic inoculation of the usual stock mixed vaccines containing pneumococci, streptococci, staphylococci, enterococci and Micrococcus catarrhalis, in concentrations of 1,000,000,000 of each per cubic centimeter. MCCLELLAND, Cleveland.

ANTITOXIC IMMUNITY IN THE COURSE OF DIPHTHERITIC INFECTION. L. BIDOLI, Riv. di clin. pediat. **34**:193 (March) 1936.

Bidoli observed the Schick reaction and the amount of antitoxin in the blood of seven children with diphtheria who received no serum, of eight who received

normal horse serum and of one hundred and thirty-seven who received antidiphtheritic serum in various amounts. The speed of the development of immunity varied in different subjects: In some it appeared in one week and in others as late as one month after injection. In patients treated by normal horse serum immunity developed more rapidly than in untreated patients but much slower than in patients to whom antitoxin was given. Small doses of diphtheria antitoxin (from 10 to 20 units per kilogram of body weight) may result in rapid immunization of the body, as indicated by the rapid change from a positive to a negative Schick reaction. Curves are given showing the amount of antitoxin in the blood of patients from each of the three groups.

HIGGINS, Boston.

ENCEPHALITIS FOLLOWING MEASLES. JESÚS ALFREDO FIGUERAS, Arch. de med. inf. **4**:168 (Sept.) 1935.

Three instances of this condition are reported by the author, with excellent pathologic descriptions. He also mentions the studies of this disease made by Cuban investigators, particularly Dr. Ramírez Corría.

SANFORD, Chicago.

POSTDIPHTHERITIC ENCEPHALITIS. CARLOS M. BARBEROUSSE and JUAN C. SUAREZ, Arch. de pediat. d. Uruguay **6**:186 (May) 1935.

Barberousse and Suarez report the occurrence of this unusual and rare condition in a child aged 4 years. Twenty-one days after a severe attack of diphtheria symptoms of cerebellar involvement accompanied by meningeal irritation developed. The spinal fluid showed a marked increase of lymphocytes. Complete spastic left hemiplegia developed following the earlier symptoms. In the opinion of the authors, encephalitis is the most probable explanation of the syndrome.

SCHLUTZ, Chicago.

PROPHYLAXIS OF WHOOPING COUGH WITH BLOOD OBTAINED FROM ADULTS AND PERSONS CONVALESCENT FROM THE DISEASE. M. QUERO MALO, Puericult. españ. **2**:23 (Feb.) 1936.

During an epidemic of whooping cough in the Provincial Institute for Child Study, passive immunization was attempted, blood from adults being used for nursing infants and blood from those convalescent from the disease for older children.

Blood from healthy adults was used in three sections of a nursery containing 120 nursing infants. Those aged 3 months and over were given from 15 to 20 cc. of mother's or wetnurse's blood intramuscularly. In section 1 the first infant who showed whooping cough infected another in the same room; both were transferred to the infirmary, and the remaining twenty-three infants were immunized at the beginning of October. After more than two months the epidemic had disappeared completely. In section 2, 25 infants were immunized and no case developed. In section 3 at the time of the immunization of 6 infants over 3 months of age the remaining 6 had already contracted whooping cough. No further cases appeared in this section, though the index of contagion from whooping cough is calculated at about 70 per cent. No child under 3 months of age contracted the disease.

Fifty older children from 1 to 4 years of age were given two intramuscular injections, a week apart, of from 7 to 10 cc. of blood from convalescent children, withdrawn during the decline of the disease in some cases and up to four weeks after its height in others. Thirteen cases had already occurred in this institution, and the only effect noted was the lessened severity of the disease occurring in those given injections, as the epidemic was not controlled.

GIFFEN, Toledo, Ohio.

PATHOLOGIC-ANATOMIC CHANGES IN THE NERVOUS SYSTEM IN POSTDIPHTHERITIC NERVOUS DISEASES. B. HECHST, Arch. f. Psychiat. **101**:1 (Nov.) 1933.

Some authors believe that the primary lesion in the nervous system in cases of diphtheria is in the peripheral nerves; others believe that it is in the spinal cord cells, and still others, that it is in the blood vessels; finally, the muscles or the terminal connections between the nerves and the muscles have been thought to be the original site of the lesion. Hechst studied five cases, in two of which death occurred and autopsy was performed during the early stages of the disease, when there were no clinical signs of postdiphtheritic changes. He reaches the following conclusions: (1) Diphtheria causes changes in the ectodermal and mesodermal elements of the central nervous system. The mesodermal changes, however, do not seem to be of great importance in the determination of the degree of change in the parenchyma. (2) In some cases changes are observed in the posterior tracts, apparently caused by lesions in the spinal ganglions. (3) The distribution of the histologic changes depends on three features: the points of entrance of the toxin, the duration of the disease and the specific affinity of special parts of the nervous system for the diphtheria toxin. (4) In the cases studied the greatest affinity for diphtheria toxin was shown by the vagus nerve, the nerve cells of the striatum and the spinal ganglions. (5) The seat of primary anatomic lesions in postdiphtheritic polyneuritis can be observed in the centers as well as in the periphery. MALAMUD, Iowa City. [ARCH. NEUROL. & PSYCHIAT.]

EPIDEMIC INFANTILE PARALYSIS. W. KELLER, Deutsche med. Wchnschr. **61**:1922 (Nov. 29) 1935.

The author gives a summary of the etiology, symptoms, prognosis, therapy and prophylaxis of poliomyelitis. Nothing new is reported. The same views are held in Germany as in the United States, except that the author still holds hope for the therapeutic use of convalescent serum. He also thinks that physical exhaustion, travel and disturbance of the respiratory and alimentary functions increase susceptibility to the disease. KERESZTURI, New York.

DIAGNOSIS AND PROPHYLAXIS OF WHOOPING-COUGH. D. GAJZÁGÓ and O. GÖTTCHE, Monatschr. f. Kinderh. **65**:141 (March) 1936.

Despite numerous improvements in method and technic, the diagnosis of early pertussis is by no means simple. The roentgen rays are, of course, of some value if they show enlarged tracheobronchial lymph nodes. The blood count has been recognized for many years. However, a count of 15,000 or more can occur in the normal infant, and lymphocyte counts can also be high without significance. The writers place value on a lymphocyte count of 50 per cent as being useful in ruling out whooping cough. Should the count be lower than that, pertussis is not to be considered. The most specific test is, of course, isolation of the bacilli, but the technic is difficult. The writers are inclined to believe that the easiest method lies in serologic tests with the complement-binding reaction.

As regards prophylaxis, they review the literature and quote the various studies of the proponents of vaccine, especially Sauer. However, they give notice that they are going to embark on an extensive study of their own, in which they will immunize a large group of children and follow them over a period of years, controlling the work with frequent serologic tests. GERSTLEY, Chicago.

EFFECT OF VITAMIN C AND ADRENAL CORTEX ON EXPERIMENTAL DIPHTHERIA. ALINE AICHAM and H. BOCK, Monatschr. f. Kinderh. **65**:289 (April) 1936.

Cevitamic acid had little effect on experimentally produced conjunctival diphtheria in the guinea-pig. Adrenal cortex likewise had little effect. When the two were combined, however, and given to animals inoculated with a culture of Corynebacterium diphtheriae there seemed to be some diminution in the severity of the infection. GERSTLEY, Chicago.

LOCAL REACTIONS WITH DIPHTHERIA FORMOLTOXOID. CARLA POHL, Monatschr. f. Kinderh. **65**:312 (April) 1936.

Thirty-one children were tested intracutaneously with formoltoxoid (a diphtheria toxin digested with formaldehyde) and fifteen with anatoxin. In from 30 to 40 per cent marked skin reactions developed, lasting about forty-eight hours. Heating the drug made no difference. The reactions were entirely independent of the results in simultaneous Schick tests. They occurred invariably in the following groups: those who had recovered from diphtheria, those who had been actively immunized and those who gave positive pseudo-Schick reactions. A higher percentage of reactions occurred in children who had been shown to have tuberculosis than in children who presented no sign of this disease.

Pohl concludes that such reactions do not depend on toxin but are allergic.

GERSTLEY, Chicago.

CRITIQUE OF THE TREATMENT AND PROGNOSIS OF POLIOMYELITIS. H. MAI, München. med. Wchnschr. **82**:1228 (Aug. 2) 1935.

Mai has not found the administration of convalescent serum useful in poliomyelitis after the onset of paralysis. Patients are not usually seen by a physician in the preparalytic stage. However, since paralysis occurred in other muscles in some of the patients whom he treated, i. e., in muscles in which the stage could be considered to be preparalytic at the time of administration of serum, he believes that serotherapy is probably of little benefit once the disease process has begun.

There are few acute diseases in which the course and ultimate result are as variable as in poliomyelitis. After three years about 10 per cent of the patients with the paralytic form are normal. The others have residual weakness or paralysis. A patient who at the onset had extensive involvement of the muscles may recover a great deal of the muscular power, so that in the end-stage the function may be as good as that of the patient who at the onset had only slight muscular weakness.

At the onset it is not possible to tell whether the paralysis of a muscle is due to edema of the cord or to actual destruction of motor nerve cells. The author does not believe that repeated lumbar puncture or roentgenotherapy relieves the edema of the cord.

Active and passive motion soon after the acute stage improves the circulation in the muscles. Splints or other apparatus should be used to prevent contractures. Such treatment should be carried out for two or three years, and only then should orthopedic procedures be considered.

BRAHDY, Mount Vernon, N. Y.

TREATMENT OF PERTUSSIS. A. KNORR, München. med. Wchnschr. **82**:1750 (Nov. 1) 1935.

Knorr tried several forms of treatment for his patients with whooping cough and obtained the best results with a vaccine which is made from many strains of pertussis bacilli, the endotoxin being completely removed.

BRAHDY, Mount Vernon, N. Y.

PROPHYLAXIS OF ACUTE INFECTIOUS DISEASES. JOSEPH SIEGL, Wien. klin. Wchnschr. **49**:275 (Feb. 28) 1936.

Joseph Siegl reviews the methods of prophylaxis used in combating various acute infectious diseases of childhood.

Diphtheria.—Specific prophylaxis has awakened the greatest interest. One must distinguish between passive and active immunization. The first is accomplished by means of antitoxin, which gives immediate protection, but the protection lasts only a few weeks, and there is danger of sensitization. Among the preparations which may be used to produce active immunization are diphtheria toxoid (anatoxin), toxin-antitoxin mixtures and flocculated toxin-antitoxin.

Scarlet Fever.—When resistance to the disease has been lowered (because of burns, wounds, chickenpox or diphtheria) convalescent serum may be used in doses of from 5 to 6 cc. for children up to 8 years of age and 10 cc. for older children. If convalescent serum is not available, scarlet fever streptococcus serum (from 10 to 20 cc.) may be employed. Attempts at active immunization have been made with scarlet fever streptococcus toxin and also with vaccines and toxoids.

Measles.—Passive prophylaxis may be attained with convalescent serum (Degkwitz), which either prevents the disease or causes it to run a mild course. If convalescent serum is not available, the serum or blood of adults who have once had measles may be used. Methods of active immunization are still in the experimental stage.

Whooping Cough.—For passive prophylaxis, convalescent serum (Debré) in doses of from 2 to 6 cc. or adult serum (Jundell) in doses of from 30 to 150 cc. may be used. Active immunization by means of mixtures of Bordet-Gengou bacilli (Haemophilus pertussis) is being attempted more and more. The vaccine is administered in several injections at intervals of a few days, the dose being increased each time. Reports on the success of prophylaxis against whooping cough are contradictory.

Chickenpox.—Prophylaxis against chickenpox need be considered only in connection with severely ill or debilitated children, or if the disease appears in endemic form in children's institutions. Convalescent or adult serum is used in passive immunization. Injections of the contents of varicella pustules (Kling) or injections of the blood of a child suffering from varicella (Késmarsky) may be used in active immunization. Attempts at prophylaxis against varicella are of doubtful value.

Poliomyelitis—Among the prophylactic measures which may be mentioned are injections of adult serum and of Pettit's serum. Numerous experiments have been made with methods of active immunization against poliomyelitis, but conclusions regarding their success cannot yet be drawn. ABT, Chicago.

STATISTICAL OBSERVATIONS ON MEASLES IN DAIREN. Y. MORITA, J. Orient. Med. **24**:22 (Feb.) 1936.

Morita's statistical analysis of 4,749 cases of measles in children received in an outpatient department during the past twenty years gave the following results:

1. The months of the year may be listed in the order of morbidity from measles as follows: April, June, March, May, January, February, December, July, November, August, October and September. The period of prevalence was from five to seventeen months. The most susceptible age was that from 1 to 2 years, the morbidity for patients 2 years of age and under being 45.1 per cent, and for those of 5 years and under, 83.1 per cent.

2. The difference in the incidence according to sex was slight, 51.6 per cent of the cases occurring in males, as against 48.37 per cent in females.

3. Koplik's spots were seen on the third day of pyrexia in 33.9 per cent of the cases, on the fourth in 26.8 per cent and on the fifth in 18.5 per cent.

4. Eruptions were observed on the fourth day of pyrexia in 32.1 per cent of the cases, on the fifth in 28.5 per cent, on the third in 14.5 per cent and on the sixth in 13.9 per cent.

5. Eruptions disappeared on the fourth day after their onset in 41.7 per cent of the cases, on the third in 16.9 per cent and on the fifth in 15 per cent.

6. Ehrlich's diazo test of the urine showed an average rate of 56.5 per cent positive reactions in the first week of eruption and an average of 27 per cent positive reactions in the second week. The acetonuria test presented the average rate of 65.4 per cent positive reactions in the first week of eruption.

7. The mortality stood at 11 per cent, (that of males being 53.3 per cent and that of females 46.7 per cent), showing again a larger percentage for males. As to age, the younger patients showed a greater percentage, the rate for those of 3 years and under reaching as high as 83.6 per cent. EDITOR'S SUMMARY.

SCARLET FEVER: XVII. SURGICAL SCARLET FEVER. F. KARLSTRÖM, Acta pædiat. **18**:287, 1936.

In the Stockholm Hospital for Infectious Diseases during the period of ten years between 1925 and 1934, of 6,375 patients with scarlet fever 97 (1.7 per cent) were classified as having the surgical variety of the infection. Analysis of the records of these patients led to the following generalizations: As regards age, the incidence of surgical scarlet fever is about the same as that of the nonsurgical type with the exception that surgical scarlet fever is somewhat more common in infants because of the greater frequency of burns of the skin during the first few years of life. The period of incubation of surgical scarlet fever is relatively short; in about 25 per cent of the cases it was forty-eight hours or less. Superficial burns predispose to the disease, whereas operations involving the throat do not. Hemolytic streptococci are found less regularly in the throats of patients at the onset of surgical scarlet fever than in the throats of patients with the usual variety of the infection; the organism can be recovered from the throat toward the end of the illness with equal frequency in both types of the disease. In surgical scarlet fever the hemolytic streptococcus is harbored more commonly in the wound than in the throat. Obvious angina as a presenting symptom is not encountered so commonly in surgical scarlet fever as in the usual variety. The frequency of complications and recurrences is the same in both types of infection. In Karlström's series scarlet fever occurred somewhat more commonly in children who had lesions of the skin than in those whose skin was intact; however, the dependability of this finding could not be confirmed statistically. Furthermore, in the Crown Princess Lovisa's Hospital for children the incidence of scarlet fever was the same in the medical and surgical wards. This observation was somewhat at variance with the conclusion that burns increase susceptibility to the surgical variety of scarlatinal infection. MCCUNE, New York.

COMPARISON BETWEEN EPIDEMIC AND ENDEMIC POLIOMYELITIS; ENDEMIC IN COPENHAGEN IN 1934. N. I. NISSEN, Ugesk. f. læger **97**:1003 (Oct. 3) 1935.

During the endemic of poliomyelitis in Copenhagen from June to December 1934, one hundred and thirty-two patients were treated. Nissen believes that the total number of cases of poliomyelitis was much higher, owing to many instances of the abortive type in which no diagnosis was made. The morbidity was relatively high among older school children and adults and was higher among men than women. A study of ninety-seven cases in the preparalytic stage showed that the symptoms of drowsiness, unrest, fibrillation, tremor, perspiration and muscular tenderness and a picture of dysphasia appeared oftener in patients in whom dementia paralytica developed after one or more days. The absolute cell count in endemic poliomyelitis, in contrast to that in epidemic poliomyelitis, is apparently not of special prognostic value. The mortality rate was lowest in infants, increasing with age. The severity of dementia paralytica and the prognosis were considerably more favorable in children at home and in school children than in persons of the older age group. ELGHAMMER, Chicago.

BLOOD PICTURE IN POLIOMYELITIS. PREBEN PLUM, Ugesk. f. læger **97**:1012 (Oct. 3) 1935.

Plum states that in poliomyelitis the white blood cell picture usually shows a slight neutrophilic leukocytosis, more marked in the severe than in the mild form, with a slight shift to the left. The leukocytosis subsides slowly. In cases of paralysis of the respiratory muscles a relatively great increase in the number of

granulated cells appears immediately before the paralysis, with a slight shift to the left and moderate increase in the absolute number of leukocytes. Similar changes were noted in three cases of poliomyelitis in which bulbar paralysis, without paralysis of the respiratory muscles, occurred. The blood picture in the nonparalytic type of poliomyelitis does not differ from that in poliomyelitis with slight paralysis. The author considers the white cell picture a valuable aid in the diagnosis of poliomyelitis in doubtful cases, especially in the differential diagnosis of pneumonia complicated with serous meningitis (meningism) and nonparalytic poliomyelitis.

ELGHAMMER, Chicago.

ENCEPHALITIS POSTVACCINALIS IN THE NETHERLAND INDIES: SOME REMARKS IN CONNECTION WITH THE ARTICLE OF K. A. SIM (AM. J. DIS. CHILD. **51**:1171 [MAY] 1936). J. H. DE HAAS and W. J. C. VERHAART, Maandschr. v. kindergeneesk. **5**:71 (Nov.) 1936.

The diagnosis in the case described by Sim is strongly doubted. With a relatively large pathologic material originating from children in the Netherland Indies who during life had shown a disease resembling encephalitis, microscopic investigation demonstrated postvaccinal encephalitis in not a single case.

VAN CREVELD, Amsterdam, Netherlands.

ENCEPHALITIS POSTVACCINALIS IN THE NETHERLAND INDIES. K. A. SIM, Maandschr. v. kindergeneesk. **5**:264 (March) 1936.

Sim replies to de Haas and Verhaart, maintaining his opinion that his case was very probably one of postvaccinal encephalitis.

VAN CREVELD, Amsterdam, Netherlands.

Acute Infectious Diseases

SPIROCHAETOSIS ICTEROHAEMORRHAGICA DEVELOPING DURING PREGNANCY. HENRI VIVNES, Progrès méd., May 30, 1936, p. 921.

Vignes points out the particularly severe course which infection with the Spirochaeta icterohaemorrhagiae takes during pregnancy. The fetus is always invaded, and abortion or premature delivery is the rule.

LESLIE, Evanston, Ill.

SYMPTOMATOLOGY AND TREATMENT OF TYPHOID IN INFANTS. JOSÉ M. DA ROCHA, Arch. de pediat., Rio de Janeiro **7**:215 (Feb.) 1936.

The following observations were made on thirty-eight children between the ages of 2 and 12 years: The most frequent symptoms were fever, bronchitis, "furry" tongue, enlarged spleen and liver, and constipation. There was no characteristic temperature curve. Blood cultures were positive in eighteen cases. The Widal reaction was positive in thirty-eight. Five patients died—one, 5 years of age, with encephalitis; one, 10 years of age, with gangrene of the lung; one, 10 years of age, with pyelitis and noma, and three, 10 years of age, with pneumonia and cardiac failure.

Among the thirty-three patients who recovered the following complications were noted: pneumonia in two; otitis in one; intestinal hemorrhage in one; pyuria in thirteen; nephritis in nine, and abscesses in one. In arriving at a diagnosis differentiation has to be made among gastro-intestinal disturbances, influenza, pneumonia, pyelitis, malaria and septicemia. A diagnosis can be made by the Widal reaction, blood culture and blood picture (leukopenia with increase of lymphocytes and diminution of eosinophils).

The treatment consists of nursing care and administration of a high caloric diet and aminopyrine. Da Rocha prefers this regimen to balneotherapy.

SANFORD, Chicago.

BACILLARY DYSENTERY IN CUBAN INFANTS. A. ABALLÍ, Bol. Soc. cubana de pediat. **8**:236 (May) 1936.

Aballí gives a detailed analysis of the dysentery syndrome from the epidemiological as well as the clinical point of view, enlarging particularly on the pathogenic effect of so-called dysentery bacilli of the Shiga, Strong, Flexner and Hiss types.

Research work carried out at the municipal hospital for children has shown that organisms of the Shiga type are the most prevalent in Cuba. Aballí believes that whenever the disease presents itself in epidemic form, organisms of this type are most likely the etiologic factor.

Large epidemic outbreaks have enabled him to study the clinical evolution of the disease as well as the histologic lesions. There are two great clinical groups —the acute and the protracted.

He reports good results with serum therapy, but is rather skeptical regarding vaccine therapy. He reports very favorable results from the use of sodium thiocyanate. He advocates repeated blood transfusions. SCHLUTZ, Chicago.

TREATMENT OF MALARIA IN CHILDREN. BRAULIO XAVIER FILHO, J. de pediat., Rio de Janeiro **3**:165 (April) 1936.

The author prefers plasmochine to quinine in the treatment of children and recommends that the dosage be as follows: 0.005 Gm. up to 1 year of age, 0.01 Gm. up to 4 years, 0.02 Gm. up to 8 years and 0.03 Gm. for older children.

SANFORD, Chicago.

Chronic Infectious Diseases

THE BACILLUS OF CALMETTE AND GUÉRIN (B C G) IN THE IMMUNIZATION AGAINST TUBERCULOSIS. SOL ROY ROSENTHAL, Illinois M. J. **69**:209 (March) 1936.

Rosenthal states that B C G by intensive studies has been shown to be avirulent and effects a sort of immunity against tuberculosis.

As the majority of persons eventually show a primary tuberculous complex caused by virulent organisms and thus a constant source of danger to the host, it would seem plausible to employ avirulent tubercle bacilli (B C G) to effect this primary infection, as by this method the disease may be constantly controlled and assayed.

BARBOUR, Peoria, Ill.

VACCINATION AGAINST TUBERCULOSIS—A COMPARATIVE STUDY IN MAN AND ANIMALS. H. J. CORPER, A. P. DAMEROW, M. L. COHN and C. B. VIDAL, J. Infect. Dis. **58**:158 (March-April) 1936.

The authors present some experimental evidence that in animals there is retardation of virulent infection, usually from a previous vaccination with viable avirulent human and bovine tubercle bacilli.

TOOMEY, Cleveland.

THE DIAGNOSIS OF PULMONARY TUBERCULOSIS IN CHILDHOOD. MILTON I. LEVINE, M. Clin. North America **19**:701 (Nov.) 1935.

The special problems arising in the diagnosis of tuberculous disease in childhood relate chiefly to the type of disease encountered at this time of life, obviously, the primary infection. However, the adult type of tuberculosis, when it does occur in early life, pursues the same course as it does in the adult. The earliest evidence of tuberculous infection is the presence of a positive tuberculin skin reaction. This may be elicited from two to ten weeks after infection occurs. The size of the reaction does not appear to indicate either the extent or the activity of the infection. Children infected with the bovine type of bacilli usually give a positive reaction with the human type of tuberculin. While cutaneous sensitivity, once established, tends to become permanent, in certain persons it may disappear in the course of

time in the absence of reinfection. The diagnosis of primary infection by the roentgen rays may be exceedingly difficult not only because of the absence of distinctive signs but also because active tuberculosis may be simulated by non-tuberculous conditions. Roentgen evidence is valueless as indicative of tuberculous disease unless the skin test is positive. The roentgen findings in the more common types of infection—primary tuberculosis, miliary tuberculosis, epituberculosis and tuberculous bronchopneumonia—are discussed.

The only absolutely positive evidence of active tuberculosis is the demonstration of the tubercle bacillus in the sputum. Since the child swallows its sputum, the necessity for examination of the washings of the stomach and examination of the feces should be more widely appreciated. The recently devised culture methods for the tubercle bacillus give promise of supplanting the inoculation of animals with material from persons with doubtful cases. The history, symptoms and physical findings, while valuable as sources of confirmatory evidence, must be interpreted strictly in the light of laboratory and roentgen findings and of the specific cutaneous reaction.

EUGENE SMITH, Ogden, Utah.

DIABETES INSIPIDUS AS A MANIFESTATION OF GENERAL MILIARY TUBERCULOSIS. J. W. HEALY, Brit. J. Child. Dis. **32**:275 (Oct.-Dec.) 1935.

The general subject of diabetes insipidus and the theories as to its causation are discussed.

A case is reported of a boy of 2½ years who had been very thirsty for two months. A culture of material from the throat showed a growth of diphtheria bacilli, but the throat showed no membrane. Diphtheria antitoxin was given, but an irregular fever persisted. The outstanding features, however, were the polydipsia and polyuria. The urine showed a trace of albumin occasionally but was otherwise normal. The lungs and heart appeared normal. Abdominal distention was controlled with solution of posterior pituitary, and this also relieved the thirst and polyuria. Meningeal signs developed, and the child died. The spinal fluid was clear and showed 37 cells but no tubercle bacilli. At postmortem examination marked external hydrocephalus was observed, with miliary tubercles scattered over both parietal lobes and over the left temporal lobe. The pituitary gland was practically completely replaced by tuberculous necrotic material.

The fact that the diabetes mellitus appeared before other symptoms and that pituitary disease had progressed to a proportionately greater extent than the tuberculous lesions elsewhere suggested that the onset of the syndrome probably coincided with the commencement of the tuberculous infiltration of the pituitary gland.

LANGMANN, New York.

RECURRING EPITUBERCULOUS INFILTRATION. I. H. ALANTAR, Arch. de méd. d. enf. **39**:171 (March) 1936.

An organism with the so-called scrofulous diathesis of Czerny which later contracts tuberculosis need not exhibit always the typical signs of scrofula. The manifestations of both disorders are revealed in an allergic state, in which predisposition must play an important rôle. In the period of infancy, scrofula presents itself often in the form of epituberculous infiltrations. These are commonly perifocal allergic reactions adjacent to primal infection and showing the usual glandular tumefaction.

This phenomenon, formerly known as splenopneumonia or the massive pneumonia of Grancher, is now designated as chronic but curable tuberculous pulmonary condensation.

The symptoms are insignificant, but roentgenographic examination shows involvement out of all proportion to the clinical findings.

A typical case of the disease in a boy of 6 is reported in detail.

AMESSE, Denver.

PREVENTION OF TUBERCULOSIS IN SCHOOL CHILDREN. J. H. TUNTLER, J. GÉNÉVRIER and H. KLEINSCHMIDT, Bull. Assoc. internat. de pediat. prevent., 1935, p. 133.

In connection with the protection of school children from tuberculosis the following points call for examination:

1. The prevalence of tuberculosis among the children. Cases of open and contagious pulmonary tuberculosis are extremely rare (the frequency being 1 in 1,500). Cases of noncontagious and serous forms are much more frequent. The diagnosis depends in the first place on periodic examination by the school physician, but all such diagnoses should be confirmed and completed by the antituberculosis dispensaries (by laboratory examination, roentgenography and other methods).

2. The child is but rarely infected by his school fellows. The danger is more often from contact with teachers and attendants, who ought to be examined periodically.

However, it will nearly always be found that the child has been infected in the family, whence arises the necessity for close collaboration between the various health services and for constant communication between the school medical inspector, the dispensaries and hospital services.

3. The child exposed to tuberculous contacts should be immediately segregated and should be placed either in an open air colony, in a family (Grancher system) or in a preventorium, according to the general state of his health.

Though today tuberculous infection in the child seems to proceed less rapidly than it did some twenty or thirty years ago and not to reach its maximum intensity until the age of 20, one still meets with a large proportion of tuberculous infection among children of school age. In cases in which evidence is available one can say that in the majority of cases this infection does not occur at school. Doubtless cases of open pulmonary tuberculosis among teachers and classmates play a certain part; one should not, however, exaggerate the importance of the notorious "unrecognized" carriers so much talked about lately. First of all, their number is less than in early childhood, and it is known that, in general, they do not infect even their brothers and sisters or their fellow boarders. In any case, on the strength of recent observations there seems to be no need to separate school children who react positively to tuberculin from those who react negatively. It is the infected adult who is the principal source of contamination, as is easily seen when all the children of a school have been given the tuberculin test and the results have been plotted on the local map. Extrafamilial sources of contamination are the more numerous.

The consequences of infection during school age are not, in general, serious. It is known that the risks are much greater in the first years of life, and one observes grave forms of pulmonary tuberculosis during the period preceding puberty and during puberty itself. It follows that the children aged from 6 to 12 years must be considered as particularly free from danger of infection. But the temporary resistance of the child does not mean that he will not fall seriously ill later.

The diagnosis is certain only when tuberculin tests are systematically and repeatedly carried out and, in case of a positive reaction, are followed by roentgen examination. Unfortunately, this sort of examination is often neglected today, except in cases in which the condition appears to be especially threatening.

Infections caused by teachers and classmates have highly variable consequences, which depend, without doubt, on the more or less frequent risks of reinfection. The resistance natural to persons of this age group may be greatly lessened by reinfection; special precautions must therefore be taken to prevent contamination by teachers and classfellows.

Student teachers must be examined before matriculation, preferably at an antituberculosis dispensary; later, when engaged in their profession, they should undergo roentgen examination about every two years. Teachers and children suffering from contagious forms of the disease should be excluded from school and readmitted only when careful examination has shown them to be incapable of infecting others. A child suffering from any form of active pulmonary tuber-

culosis should be considered preferably as contagious. Funds will have to be found to compensate teachers thus dismissed and school instruction arranged for tuberculous children in sanatoriums.

It is much more difficult to avoid infection out of school. Perhaps it is not even desirable for persons at this age to eschew all risk of contagion. One ought rather to pay attention to the problem of reinfection from family and household sources.

To insure the right kind of environmental prevention the mass of the population will have to be educated, and that can best be done by beginning early, at school, with simple lessons.

In the matter of individual prevention, the bettering of economic and health conditions will be aimed at. In the selection of children for holiday camps or sanatoriums too much attention should not be paid to children of the age group in which there is the greatest resistance to tuberculosis, but rather to those of preschool age and to those who have reached the age of puberty. Consequently one must consider only the children suffering from active tuberculosis who have obviously been recently infected and who are permanently exposed to the disease or whose general health has been affected by the disease or by underfeeding. The length of the stay must be sufficient, and advantage should also be taken of the winter months. Additional food will increase the resistance of the infected children left at home, who will also be benefited by day camps, by air and sun baths and by treatment with ultraviolet rays.

AMESSE, Denver.

TUBERCULOSIS IN 1936. P. LEREBOULLET and H. GAVOIS, Paris méd. **1**:1 (Jan. 4) 1936.

This article reviews the progress in the study and control of tuberculosis made in the past year. It is divided into four sections: (1) the fight against tuberculosis, (2) biologic studies, (3) clinical studies and (4) prophylaxis and therapy.

LESLIE, Evanston, Ill.

DEFINITION OF PERIFOCAL INFILTRATION AND EPITUBERCULOSIS. R. BENDA and M. MOLLARD, Paris méd. **1**:4 (Jan. 4) 1936.

The authors add nothing to the understanding of either perifocal infiltration or epituberculosis, stating only that epituberculosis is a particular form of perifocal infiltration in which the congestive reaction is so vast and the principle focus so small that the former is responsible for the semeiologic manifestations. They have found that epituberculosis may occur in any stage of the disease, even in an adult whose disease is principally of the chronic ulcerative type.

LESLIE, Evanston, Ill.

PROTECTION OF THE SCHOOL CHILD AGAINST TUBERCULOSIS. J. GÉNÉVRIER, Paris méd. **1**:13 (Jan. 4) 1936.

This study shows that contact with other school children is a rare source of contagion in tuberculosis. It is contact in the family which is nearly always responsible for tuberculosis in the school child. Nevertheless, measures of protection must include examination of pupils and of teachers and other employees of the school.

LESLIE, Evanston, Ill.

SYNDROME OF CAVITATION IN ULCEROCASEOUS TUBERCULOSIS OF THE INFANT. TEODOSIO VALLEDOR, Bol. Soc. cubana de pediat. **8**:11 (Jan.) 1936.

The author reports observations of the condition described in the title in twenty-six infants ranging in age from 2 to 30 months. It is noted in nearly 25 per cent of autopsies on infants. In these cases there is always massive infection in the environment.

The cavities may occur in the primary lesions or may be secondary in the course of tuberculous bronchopneumonia. The number, size, location and shape of the cavities is variable; generally they are single and unilateral and located in the middle or inferior lobe of the right lung.

Roentgen examination offers the best means of detection of the cavity. In the infant the cavity often shows no definite wall. Hemoptysis is a rare symptom in infants. Vomiting of necrotic material is not common. Pneumothorax is the most common complication. The condition usually has a fatal termination.

SCHLUTZ, Chicago.

HEMATOGENOUS FASCIAL TUBERCULOSIS IN A NINE YEAR OLD BOY. CARLA POHL, Monatschr. f. Kinderh. **65**:279 (April) 1936.

Pohl reports multiple symmetrical metastatic tuberculosis in the subfascial tissues of a 9 year old boy. Surgical operation was not employed. The patient recovered under general treatment.

GERSTLEY, Chicago.

TUBERCULIN PATCH TEST. K. ANDO, J. Pediat. (Tokyo), no. 424, Sept. 20, 1935, p. 1300.

Ando classifies the percutaneous tuberculin tests into:

1. Friction method: (*a*) tuberculin ointment (Moro); (*b*) undiluted tuberculin (Lignier, Wegerer, Lovett).

2. Contact method: (*a*) tuberculin ointment (Habetin); (*b*) diluted tuberculin with water (Lautier and Kasahara) or plaster application (Blumenau and others).

The author used the method employing adhesive plaster, and the results compared favorably with those of the Mantoux and the Pirquet test carried out simultaneously. This method is recommended as being the simplest and most convenient.

KATO, Chicago.

ON THE DECREASE IN TUBERCULOUS MENINGITIS. A. WALLGREN, Acta pædiat. **18**:474, 1936.

This paper constitutes Wallgren's reply to Allen Gunther's criticism of the article of Wallgren and Nilssen which appeared in the *Revue française de pediatrie* (**11**:37, 1935). Gunther's attack was published in the *Acta pædiatrica* (**18**:340 [March 16] 1936) and abstracted in the AMERICAN JOURNAL OF DISEASES OF CHILDREN.

Wallgren and Nilssen called attention to the recent decrease in the number of cases of tuberculous meningitis which has occurred in Gothenburg, Sweden, ascribing the diminished mortality, in part at least, to the public health measures undertaken in an intensive attempt to control tuberculous infection. Gunther admitted the fact but denied that the credit was due to specific prophylactic agencies. He contended that similar improvement has been recorded in communities where formal steps have not been taken to check the spread of tuberculosis. He ascribes the diminution in the number of cases of tuberculous meningitis to the general decline of the death rate from tuberculosis among persons of all ages; also, to the falling birth rate, which leads to a decrease in the size of the susceptible group. In retaliation Wallgren points out certain defects in Gunther's data and certain statistical errors in the latter's paper which render his criticism ill founded. Asserting that both Gunther and he see eye to eye with reference to the principles underlying the prevention of infantile tuberculosis, he regrets Gunther's deprecatory attitude toward the work of the clinics for tuberculosis; such an attitude, if stoutly maintained, will undermine the enthusiasm on which the continuation of much fruitful public health work is dependent.

This is one of those pleasant polemics which from time to time enliven the European literature and which make contemporary American periodicals seem somewhat stern by comparison.

MCCUNE, New York.

OCCURRENCE OF TUBERCLE BACILLI IN SECRETION OF FASTING STOMACH OF CHILDREN. G. J. HUËT, Maandschr. v. kindergeneesk. **5**:149 (Jan.) 1936.

Huët gives the results of a careful examination (by Dr. Boer and Dr. Ruys) for tubercle bacilli in the gastric lavage of children under treatment in a sanatorium for so-called closed pulmonary tuberculosis. Each sputum was tested on eight Löwenstein mediums and in one guinea-pig.

Among the children with tubercle bacilli in the gastric contents two groups could be distinguished: (1) infants and children apparently still suffering from a primary infection and (2) children with advanced pulmonary tuberculosis. In the first group of children it seemed that the excretion of bacilli was a frequent sign. Among the children in this group (aged from 1 to 10 years) bacilli were found as follows:

Classification	Children with Bacilli Present in Gastric Contents
54 children with active tuberculosis	36 (66.6%)
26 children with activity dubious	12 (46 %)
49 children with inactive tuberculosis	18 (36 %)

Children of this type must be considered as having a contagious disease, though there are several reasons to believe that under normal conditions the contagiousness is not great. Many authors agree that contagiousness can increase when coughing occurs, even when this is caused by nonspecific infections of the upper respiratory tract, and when vomiting and other signs occur. In the majority of cases (twenty-four) the bacilli disappeared within from fourteen to fifteen months after the clinical onset; five children did not lose their bacilli until after a lapse of from nineteen to twenty months. In four patients the bacilli are still present; in one of these a maximum of forty months has been attained, counting from the beginning of the disease. Among children of the second group (aged from 10 to 18 years), with advanced tuberculosis, bacilli were found as follows:

Classification	Children with Bacilli Present in Gastric Contents
50 children with active tuberculosis	37 (74%)
8 children with dubious activity	5
8 children with inactive tuberculosis	3

Thus among 50 children with apparently closed active advanced pulmonary tuberculosis 74 per cent showed bacilli in the contents of the empty stomach. Cases of this type of tuberculosis must be considered as far more dangerous, as this type often precedes open pulmonary tuberculosis with a roentgenoscopically visible cavity. Also coughing is a frequent symptom in cases of this type.

Therefore the quantity of the bacilli, as well as the probability that they will not be swallowed but expectorated by coughing, leads Huët to maintain that, compared with the danger of cases of primary infection, the contagiousness in these advanced cases will be far greater. VAN CREVELD, Amsterdam, Netherlands.

Diseases of Blood, Heart and Blood Vessels and Spleen

ELECTROCARDIOGRAMS ON 167 AVERAGE HEALTHY INFANTS AND CHILDREN. C. T. BURNETT and E. L. TAYLOR, Am. Heart J. **11**:185 (Feb.) 1936.

A study was made of 1,276 electrocardiograms obtained from 167 healthy children, ranging in age from 3 weeks to 12 years.

The individual variations in the electrocardiograms were greater than those of the present accepted standards for the electrocardiogram of the normal adult.

The amplitude of the P wave was higher and lower than that in the tracing for the normal adult. Notched forms occurred in all leads. R waves were also found to show greater variation in height than is considered normal in the adult. Slurring of the R wave was found in 36 per cent of the records and notching in about 4.5 per cent. Right axis deviation was frequent in the first three months of life. Left axis deviation was occasionally noted in the tracings of healthy children.

GIBSON, Chicago.

TETRALOGY OF FALLOT (EISENMENGER TYPE) WITH HYPOPLASIA OF THE DEXTROPOSED AORTA. J. E. TALLEY and K. FOWLER, Am. J. M. Sc. **191**:618 (May) 1936.

A case is reported demonstrating the tetralogy of Fallot (pulmonary stenosis, interventricular septal defect, deviation of the origin of the aorta to the right and hypertrophy of the right ventricle). Fallot first published a series of articles on the subject in 1888. The present case was observed in a woman of 31 years, who was born prematurely at 8 months and was a "blue baby." She developed normally both mentally and physically, passed through two pregnancies and took care of her own house to within a month of her death. The diagnosis was confirmed at autopsy, and in addition there was hypoplasia of both the thoracic and the abdominal aorta.

HENSKE, Omaha.

COARCTATION OF THE AORTA WITH INTERMITTENT LEAKAGE OF A CONGENITAL CEREBRAL ANEURYSM: REPORT OF A CASE. T. W. BAKER and W. D. SHELDON, Am. J. M. Sc. **191**:626 (May) 1936.

A case is reported in a young woman of 25 years, still living. An outline of diagnostic signs is given, and the pathology of the anomaly is discussed. According to a statement, an unusually large number of consecutive necropsies indicated that coarctation of the aorta occurs far more frequently than is clinically appreciated.

HENSKE, Omaha.

EARLY INCIDENCE OF SPONTANEOUS MEDIAL DEGENERATION ("ARTERIOSCLEROSIS") IN THE AORTA OF THE RABBIT. H. D. KESTEN, Arch. Path. **20**:1 (July) 1935.

These experiments were undertaken to reproduce in the arteries of rabbits the lesions that have been reported as presumably transmitted by mothers that have received viosterol to their young (Junck, A.: *Virchows Arch. f. path. Anat.* **283**:265, 1932). The rabbits used were the successive litters of several mothers by a single father.

Spontaneous medial degeneration was observed in 54 per cent of 125 rabbits. No significant difference between the young of treated and untreated mothers was demonstrable. Furthermore, lesions were found at the age of 10 days, and the incidence increased to 87 per cent at the age of 8 months.

APFELBACH, Chicago.

EXPERIMENTAL CHOLESTEROL ARTERIOSCLEROSIS AND ITS RELATIONSHIP TO HUMAN ARTERIOSCLEROSIS. G. LYMAN DUFF, Arch. Path. **20**:81 (July); 259 (Aug.) 1935.

This comprehensive review of the experimental production of cholesterol arteriosclerosis covers the history of this form of experimentation, descriptions of the gross and microscopic experimental lesions and observations relating to the differences between spontaneous and experimental arteriosclerosis in rabbits, the alterations in the arteries of birds and mammals from excessive ingestion of cholesterol and the remote anatomic effects of this experimental method.

In addition, Duff draws conclusions from his experiments, among which are: Some injury to the arterial wall is the primary event in the development of experimental cholesterol arteriosclerosis in rabbits. There are important differences between arteriosclerosis in man and the lesions occurring in experimental cholesterol arteriosclerosis. In spite of the normal differences between man and rabbits which might be used to explain the differences in the two diseases, there is no valid reason to believe that excess of cholesterol in the diet plays any rôle in the causation of arteriosclerosis in man.

In addition to the account of the experiments of the author, the excellent description of previous studies made by this experimental method is recommended.

APFELBACH, Chicago.

EFFECT OF IODINE ON CHOLESTEROL-INDUCED ATHEROSCLEROSIS. DOROTHY R. MEEKER, H. D. KESTEN and JAMES W. JOBLING, Arch. Path. **20**:337 (Sept.) 1935.

The experiments were directed toward studying the therapeutic effects of iodine on cholesterol-induced atherosclerosis in rabbits. Potassium iodide was administered with the food for from one to three months. The authors were unable to observe any influence on the rate or on the nature of the involution of the vascular lesions.

APFELBACH, Chicago.

SPONTANEOUS ARTERIOSCLEROSIS IN RATS. W. C. HUEPER, Arch. Path. **20**:708 (Nov.) 1935.

The important organs of seventy-five adult white rats were examined for arteriosclerosis. In the small and medium branches of the pulmonary artery, subendothelial cone-shaped calcified foci were found, most frequently near the bifurcations. Occasionally the media was also involved. Similar lesions were not found in the arteries of other organs.

APFELBACH, Chicago.

ESSENTIAL HYPERTENSION IN BOY OF TWO YEARS OF AGE. HELEN B. TAUSSIG and DOUGLAS B. REMSEN, Bull. Johns Hopkins Hosp. **57**:183 (Oct.) 1935.

When first seen a boy showed cardiac enlargement and cardiac failure, indicating that hypertension had existed for some time. He was observed for eight months, during which time the blood pressure was 130 systolic and 100 diastolic in both the arms and the legs. Detailed studies gave no adequate explanation for the persistent hypertension. Cardiac failure was progressive to death. At autopsy the lesions in the kidney (slight scarring along the cortical margins) were different from the arteriolar and glomerular changes usually associated with hypertension, but the case was considered to be one of essential hypertension.

LYTTLE, New York.

PURPURA IN CHILDREN. CARROLL M. POUNDERS, South. M. J. **29**:317 (March) 1936.

Thrombocytopenic purpura appears to be a form of primary blood dyscrasia in which the relation to the platelets is similar to that of pernicious anemia to the erythrocytes. The disease occurs in both the acute and the chronic form, and its etiology is unknown. The diagnosis depends on the finding of a low platelet count, normal clotting time, prolonged bleeding time and nonretractility of the clot. The acute form may terminate by recovery or death, or it may become chronic. The chronic form seems to be more common in females. The giving of repeated blood transfusions is a valuable measure for prolonging life but does not appear to be curative. The only effective remedy is splenectomy. This is indicated in both the chronic and the acute forms, especially in instances in which repeated blood transfusions have been given. It should be performed only after thorough study of the blood has established the diagnosis beyond question.

SCHLUTZ, Chicago.

SPLENECTOMY FOR THROMBOCYTOPENIC PURPURA. GWENDOLINE SMITH, Brit. M. J. **1**:157 (Jan. 25) 1936.

Smith gives the following conclusions:

"1. A case of acute purpura haemorrhagica in a woman of 41 years is recorded. Splenectomy was successfully performed, and the patient remains in very good health fifteen months after operation.

"2. The immediate and remote results of splenectomy for this condition are discussed.

"3. Conclusions based on published cases show that splenectomy is certainly indicated in acute cases with severe bleeding, and delay in operating adds to the operative risks. In chronic cases splenectomy should be considered in all except the mild ones, but though the immediate mortality rate is much lower, permanent cure cannot be expected in every case."

ROYSTER, University, Va.

STOVARSOL (ACETARSONE) IN THE TREATMENT OF CONGENITAL SYPHILIS. H. S. MITCHELL, Canad. M. A. J. **33**:377 (Oct.) 1935.

The following dose of acetarsone is recommended: 5 mg. per kilogram of body weight each day for one week; 10 mg. per kilogram a day, the second week; 15 mg. per kilogram a day, the third week, and 20 mg. per kilogram a day until the ninth week. A rest of six weeks is given, and the course is repeated, irrespective of the serologic reaction. Better absorption is obtained if the drug is given one-half hour before meals in water or milk.

The results are as good as those obtained with neoarsphenamine; the toxic manifestations are less severe, and the ease of administration insures better cooperation on the part of the parents and consequently more thorough treatment and extended observation.

MOORE, Omaha.

THE TREATMENT OF CONGENITAL SYPHILIS WITH STOVARSOL. A. M. DAVIDSON and ARTHUR H. BIRT, Canad. M. A. J. **34**:33 (Jan.) 1936.

Fifty-one patients with congenital syphilis were studied through the outpatient department of the Winnipeg Children's Hospital, and thirty-seven patients with this condition were treated with acetarsone, administered by mouth.

With acetarsone therapy, more than twice as many cures were obtained in one-third the time required with methods employed prior to the use of acetarsone. Only three patients had mild toxic symptoms. This method offers the following advantages over other forms of treatment: simplicity of exhibition, regular attendance at the clinic, fewer toxic effects and reduced cost of treatment.

MOORE, Omaha.

TWO CASES OF ENDOCARDITIS IN INFANTS. E. S. GIDDINGS, Canad. M. A. J. **35**:71 (July) 1936.

1. An infant which died at the age of 2 months had been subject to cyanotic spells beginning at the age of 2 weeks. The cyanosis and difficulty in respiration increased until death. Postmortem examination showed subacute bacterial endocarditis with terminal bronchopneumonia.

2. In one of new-born twins cyanosis and difficult respiration developed on the fourth day. Physical examination of the heart at this time revealed nothing abnormal. The postmortem investigation showed pneumococcic endocarditis.

MOORE, Omaha.

CONGENITAL CARDIAC HYPERTROPHY. ROBERT DEBRÉ, JULIAN MARIE and J. BARNARD, Arch. de méd. d. enf. **39**:98 (Feb.) 1936.

Debré, Marie and Barnard report the case of an infant with an excellent family history and in normal health for fifteen days after birth who suddenly was seized with convulsions. These attacks occurred daily and lasted for three or four minutes, to be followed by natural sleep. The child was first seen by the family physician, who found a mesocardiac systolic murmur, suggesting Roger's syndrome. At the time of the examination by Debré and his associates, Nov. 13, 1934, a very loud systolic souffle could be heard over the entire precordial region; the pulse rate was 140 and the respirations 68, although the infant was apyretic; the spleen was easily palpable, and auscultation of the lungs was without result. There was retraction of the epigastric region on inspiration. Roentgenologic surveys revealed an enlarged heart, globular in shape and drawn to the left, with an

obscurity in the upper part of the left lung. The diagnosis of Roger's disease was confirmed, and the convulsions were attributed to some error in cerebral development accompanying that of the heart. During the next three weeks the seizures disappeared, and the patient seemed to enjoy normal health. On December 8 the infant suffered a severe attack of dyspnea; the convulsions returned, and death ensued two days later. During this terminal attack a definite diagnosis of congenital hypertrophy was made. Autopsy showed an enormously enlarged thymus and marked hypertrophy of the heart without valvular involvement.

In the discussion of the origin two hypotheses are offered, which might with equal force be presented in explanation of a similar congenital hypertrophy of the pylorus. The first theory concerns defects of metabolism, especially of that of glycogen and fat, with a deposit of such substances in the muscle fibers; the second assumes that trophic disturbances provoked local hypertrophic reactions.

AMESSE, Denver.

VARIATION IN THE VISCOSITY OF THE BLOOD AND SERUM IN VARIOUS MORBID STATES OF INFANCY. EMIL HURMUZACHE and ELISE SAPIRA, Bull. Soc. de pédiat. de Iasi **6**:61 (April-June) 1935.

Studies were made on 100 children under 3½ years of age. Viscosity of the whole blood was found to be increased in moderate malnutrition and in rickets. The variation in viscosity of the blood in other conditions showed no consistency. The degree of viscosity varied directly with the hemoglobin content. Variations in the viscosity of the serum were too small to be of any significance.

LESLIE, Evanston, Ill.

PREVENTION OF LATE MANIFESTATIONS AND RELAPSES IN CONGENITAL SYPHILIS. E. LESNÉ and A. LINOSSIER-ARDOIN, J. de méd. de Paris **55**:1096 (Dec. 12) 1935.

After the report of three cases in which late manifestations of syphilis occurred, the authors formulate the following rules: (1) The ideal preventive procedure is treatment of the parents, particularly of the mother during pregnancy; (2) when this has not been carried out and the child is born without apparent stigma, preventive treatment of the child is necessary; (3) when a child presents a syphilitic lesion, intense and prolonged treatment (five years) is necessary to assure its future; (4) the finding of syphilis in a child should demand clinical and serologic examination of the brothers and sisters.

LESLIE, Evanston, Ill.

HEART DISEASE IN 1936. PAUL HARVIER and ROGER BOUCOMONT, Paris méd. **1**:361 (May 2) 1936.

This is a review of the literature for the year 1936 on disturbances of the cardiovascular system. Numerous references are given. The body of the article consists of brief statements concerning observations by various authors.

LESLIE, Evanston, Ill.

ANEMIAS OF INFANCY. MAURICE LAMY, Rev. méd.-sociale de l'enf. **4**:1 (Jan.-Feb.) 1936.

The author divides the anemias of infancy into two classes: (1) simple anemias and (2) those of the von Jaksch type. The former are characterized by a lowering of the color index with or without a decrease in the red blood cell count; the latter, by a marked decrease in both the red cell count and the percentage of hemoglobin, with the color index keeping near 1, and by splenomegaly and a marked reaction of the marrow. He considers the causes to be the same for both, viz., hemorrhages, infections, parasites, digestive disturbances and dietary deficiency.

BROWNE, Detroit.

THE THROMBOCYTOPENIC PURPURA OF WERLHOFF. ALEJANDRO VOLPE, Arch. de pediat. d. Uruguay **7**:405 (Sept.) 1935.

Volpe reports a case of thrombocytopenic purpura in a child aged 4 years. The manifestations began at 8 months, were followed by a second fairly mild attack and finally by an extremely severe attack at 4 years. All the purpuric symptoms were cutaneous. Absolute thrombopenia was present, and the bleeding time was extraordinarily increased. Complete cure was effected by subcutaneous injection of the father's blood.

SCHLUTZ, Chicago.

NEW STUDIES OF CLINICAL FEATURES AND PATHOGENESIS OF NIEMANN-PICK'S DISEASE. T. BAUMANN and M. ESSER, Schweiz. med. Wchnschr. **66**:6, 1936.

The clinical, laboratory and pathologic observations in a case of Niemann-Pick's disease, thoroughly studied over a period of six months, are presented by Baumann. The blood cholesterol content was normal in amount; the phosphatide content was slightly decreased. The excretion of cholesterol was from ten to twenty-five times that in a normal child, and the cholesterol content of the bile was seven times the normal amount. The retention of nitrogen varied remarkably, being 72 per cent in one period and 1 per cent in another. On pathologic examination all the tissues except the skin contained large numbers of Pick's cells. The bones and muscles showed marked mineral impoverishment, whereas the skin, the only tissue histologically free from disease, was overladen with minerals and seemed to act as a mineral depot.

Esser describes the morphologic and bacteriologic findings in the blood of this patient. Basophilic reticulum cells occurred in proportions of about 2 per cent of the total leukocyte count. Reticular giant cells from 45 to 55 microns in diameter, seen singly on the smears, are described for the first time. Many of these cells contained cocci, usually diplococci, less often single. These cocci could not be seen in other cells or extracellularly. Foam cells in the peripheral blood were another unusual observation. These three types of cells and also the intracellular cocci were likewise observed in a case of Schüller-Christian's disease.

Wieland, in discussing these observations, agrees with Baumann's view that the pathologic process in Niemann-Pick's disease is probably not an overproduction of lipoids with secondary deposition in the reticular and parenchymal cells, as conceived by Pick, but rather a general injury to the cells, an "endogenous dysfunction," with excretion of products of degeneration into the body of the cell, a theory expressed before that of Pick by Schlagenhaufer, Kraus and Aschoff. Wieland considers it not improbable that an etiologic relationship exists between the cocci discovered by Esser and the disturbances of the reticulo-endothelial system.

CRANE, Chicago.

NATURE OF THE PHOSPHATIDES AND OTHER LIPIDS IN THE BRAIN AND LIVER IN NIEMANN-PICK DISEASE. A. KLENK, Ztschr. f. physiol. Chem. **235**:24, 1935.

It was previously reported that there is a great increase in the sphingomyelin content of the spleen in Niemann-Pick disease. The content of lecithin and cephalin fractions was very small. In the study of a case of this condition the brain and liver were also found to contain an unusually high content of sphingomyelin. The glycerophosphatides (lecithin and cephalin) showed a high content in the liver, although in both the spleen and the liver these values are probably in the upper limit of normal. In the brain the high sphingomyelin content was in marked contrast to the almost complete lack of cerebrosides. The sphingomyelin in both the spleen and the liver in this case of Niemann-Pick disease was composed of a mixture of lignoceric acid, nervonic acid, stearic acid and palmitic acid compounds. However, in the brain there was almost a pure stearosphingomyelin. This is the first time that the isolation of such a pure substance from the brain has been successful. On the other hand, there was a lack of C_{24} acids, which seemed to be unusual.

A discussion of the relationship of these findings to those in amaurotic family idiocy (Tay-Sachs disease) and in Gaucher's disease is given. The steps in the analyses of the various fractions are given in detail, with a discussion of the possible significance.

HANSEN, Minneapolis.

REPORT OF A CASE OF AGRANULOCYTOSIS IN AN ELEVEN YEAR OLD GIRL. IRENE BALUKIEWICZ, Pedjatrja polska **15**:123, 1935.

Agranulocytosis occurs rarely in children. The condition in this case was diagnosed as diphtheria until the blood count was taken. The etiology and pathogenesis of this malady are not clear. However, there are usually injuries to the red bone marrow. Agranulocytosis was described by Schultz in 1925 as a disease entity.

KRUPINSKI, Chicago.

TRANSFUSION OF STORED BLOOD. G. G. KARAVANOV, Vrach. delo **18**:131, 1935.

Karavanoy discusses the problem of transfusion of stored blood and presents his clinical observations on 102 patients who received transfusions by this method.

A study was made of the following problems:

1. The clinical reaction of the patient to the transfusion of stored blood.
2. The influence of this method of transfusion on the course of the disease.
3. The influence of preserved or stored blood on the qualitative and quantitative composition of the blood of the recipient.

The conclusions were as follows:

1. The transfusion of stored blood may find clinically a wide usefulness. This method is of value particularly in emergencies.
2. Shortly before transfusing the blood must be checked thoroughly for hemolysis, and for sterility. Hemolysis, however slight, is a contraindication to its use.
3. The proposed method of obtaining a sample of blood for examination prevents secondary contamination of the remaining portion of the blood.
4. A definite general stimulation follows the transfusion of stored blood.
5. The optimum period of preservation is one under from six to seven days.
6. Transfusion of stored blood cannot replace other methods of blood transfusion in all cases, but it is a valuable supplement, particularly for immediate transfusions.

BODER, Los Angeles.

DIAGNOSIS OF ENDOCARDITIS. E. A. CHERNIKOV and O. BORTZ, Vrach. delo **18**:211, 1935.

Chernikov and Bortz discuss the present status of the diagnosis of endocarditis and propose a new procedure to aid in making the differential diagnosis between so-called endocarditis simplex and other forms of endocarditis.

They believe that the diagnosis of endocarditis is made too frequently, and that, although there are no pathognomonic signs or symptoms of endocarditis, a low grade fever is present most constantly and is characteristic of the disease.

The new diagnostic procedure is based on the observation that a relative lymphocytosis is usually characteristic of the blood picture in endocarditis simplex, whereas neutrophilia is most frequently present in the septic form of endocarditis. Since the aforementioned blood picture is usually present but not always sufficiently obvious, the authors devised a method which brings out more distinctly the characteristic leukocytic reaction. This procedure consists in a subcutaneous or intradermal administration of an antigen which, by producing a reaction against foreign protein, brings forth more distinctly the characteristic lymphocytic response in endocarditis simplex. Milk in quantities of from 3 to 5 cc. administered subcutaneously was used most successfully as an antigen. Differential counts were made on the blood of the patients who were fasting previous to the injection, then

from two to three hours after the injection and finally twenty-four hours after the injection—all before breakfast.

The results obtained demonstrated that twelve of sixteen patients whose condition was clinically diagnosed as endocarditis simplex, or 75 per cent, had pronounced leukopenia with relative lymphocytosis after the injection. The test was done likewise on forty-three patients with other forms of endocarditis.

In patients with acute rheumatic fever as well as in those with septic endocarditis the reaction was most frequently that of slight leukocytosis with relative neutrophilia, while in patients with the subacute forms of articular rheumatism the reaction was variable.

The authors' conclusions are as follows: 1. In patients with endocarditis simplex the most frequently observed reaction following subcutaneous administration of milk is that of relative lymphomonocytosis, with a variable degree of leukopenia. 2. A leukocytic reaction characteristic of a disease can frequently be reinforced and made more obvious by the administration of an antigen such as milk, thus aiding in the diagnosis of a disease. BODER, Los Angeles.

THREE CASES OF INFANTILE LEUCEMIA. H. MURATA, J. Pediat. (Tokyo), no. 428, Jan. 20, 1936, p. 88.

Three cases of leukemia in infants observed by the author in ten years are reported. The first case was one of acute myeloblastic leukemia in a 4 month old boy with a maximum leukocyte count of 96,200, of which 73 per cent were myeloblasts. The second case was one of subacute myeloid (mixed cell type) leukemia in a 5 month old boy with a maximum leukocyte count of 169,600, of which 5 per cent were myeloblasts and about 80 per cent were neutrophilic granulocytes in all stages of development. The third case was one of acute lymphatic leukemia in a 4 month old boy with a maximum leukocyte count of 227,200, of which all cells belonged to three varieties of lymphocytes. Only in the last case is the confirmatory diagnosis based on postmortem examination given. The first two patients were treated by roentgen irradiation. The duration of the disease was one month in the first and third cases and two months in the second.

KATO, Chicago.

THE ELECTROCARDIOGRAM OF THE PREMATURE INFANT. C. E. RÄIHÄ, Acta pædiat. **18**:440, 1936.

Räihä reports the results of serial electrocardiographic examinations of forty-five premature infants; some of the infants were followed for several months. He agrees with the conclusion of previous investigators that the electrocardiogram of the premature infant is not a typical one. As the infant grows older the complexes assume greater amplitude. This phenomenon may depend on developmental changes in the relative force of the two halves of the heart or on changes intrinsic in the heart muscle itself. In the premature infant the alpha angle is smaller during the first weeks of life than it is in the full term infant of the same age; the magnitude of the angle decreases more slowly in the premature than in the full term infant. In seventeen of the patients certain irregularities were observed in the formation and conduction of the electrical impulses; these were of an ephemeral nature and apparently did not depend on infection or on disease of the myocardium. They were thought to be of reflex origin and to be related to the position of the heart as well as to peculiarities in the structure of the myocardium and of the coronary system which are common in premature infants. The paper is copiously illustrated and contains a brief bibliography.

MCCUNE, New York.

PAROXYSMAL TACHYCARDIA AND BUNDLE BRANCH BLOCK IN A BOY OF ELEVEN. N. FAXÉN, Acta pædiat. **18**:491, 1936.

Although adults who suffer from paroxysmal tachycardia usually state that their attacks began in childhood, only about thirty-five cases of this condition in

children have been reported in pediatric literature. It is possible that this discrepancy may result from the fact that the attacks in children are often relatively asymptomatic. Paroxysmal tachycardia is usually a manifestation of organic disease of the heart, although occasionally it is the result of pathologic conditions outside the heart, such as elevation of the diaphragm, encephalitis, irritation of the vagus nerve and pertussis; it is not commonly a consequence of acute rheumatic fever. Four mechanisms are described: auricular, ventricular and nodal tachycardia and auricular flutter. Some writers assert that auricular extrasystoles, auricular tachycardia and auricular flutter are closely allied from a functional point of view, although pathogenically somewhat dissimilar. The symptomatology may be meager; infants usually exhibit slight cyanosis during the attacks; loss of consciousness may occur. Children usually tolerate the illness well, although sudden death may occur from embolism. The disease is compatible with long life. It is generally agreed that manifestations of myocardial insufficiency indicate a poor outlook. Electrocardiographic examination is of the highest importance in establishing a prognosis.

Faxén reports the case of an 11 year old boy who had recently suffered from an illness resembling acute rheumatic fever. The onset of paroxysmal tachycardia was announced by palpation, which commenced suddenly and terminated abruptly several times during the few weeks preceding entry into the hospital. On admission the boy exhibited only pallor, a heart rate of 220, slight cardiac enlargement and a harsh short apical systolic murmur. The electrocardiogram showed a rapid rate and alteration of the complexes, suggesting bundle branch block. The attack subsided suddenly without treatment on the day after admission. The electrocardiograph showed improvement but did not show a return to normal. However, no similar episodes were noted during the subsequent few months of observation. It was felt that the underlying lesion was a combination of congenital heart disease with superadded acute rheumatic infection.

McCune, New York.

Increase in Reticulocytes Following Injection of Anemic Serum. Erling Hjort, Norsk mag. f. lægevidensk. **97**:270, 1936.

Intravenous injection of serum from rabbits recently bled produced in one third of the animals receiving the injection an increase of the percentage of reticulocytes. This increase corresponded to that usually seen after considerable hemorrhage. Anemic serum from one and the same rabbit may in two other animals give a considerable increase in the number of reticulocytes in one and no particular increase or even a fall in the other.

The great increase in the number of reticulocytes was not followed by a corresponding increase in that of the red corpuscles.

Toverud, Oslo, Norway.

Diseases of Lungs, Pleura and Mediastinum

An Analysis of Three Hundred Cases of Asthma in Children. Edward Scott O'Keefe, New England J. Med. **214**:62 (Jan. 9) 1936.

The average age of the patients at the time of examination was 7 years and 9 months. Between twenty and fifty tests with protein were made on each child, the common food, animal and pollen allergens being used. The scratch method was most commonly employed, although in the last year many of the tests with pollen and animal emanations were made by the intradermal method as well. The combined methods gave positive results in a much higher percentage of cases of pollen disease than when the scratch method alone was used.

In about 10 per cent of the patients the onset of the asthma was in the first year, and in 12 per cent, in the second year. In 66 per cent the asthma began during the first six years. The average age at onset for the entire group was 4.6 years.

In 38 per cent of the cases there was a family history of allergy, and in 28 per cent of these cases the asthma was complicated with eczema, hay fever or other allergic conditions. Of patients having a negative family history, 23 per cent showed allergic conditions complicating the asthma. Of the children with a positive family history, 30 per cent, and of the group with a nonallergic family history, 34 per cent, showed multiple sensitization.

An analysis of the cases in allergic families showed that one or both parents were allergic in 40 per cent of the cases; in 37 per cent the grandparents had been allergic; in 16 per cent the brothers or sisters were allergic. In this group, the relatives showed asthma in 53 per cent of the cases, hay fever in 26 per cent, eczema in 13 per cent, urticaria in 1.5 per cent, migraine in 1.5 per cent, vasomotor rhinitis in 1 per cent. Asthmatic parents transmit a tendency toward asthma rather than a tendency toward one of the other allergic conditions.

A chart shows foods and animal emanations to be of about equal importance during the second year. From the second year on, for several years, the animal emanations become more important and the foods less important. Pollens remain comparatively unimportant until the ninth year, when they are found to show the highest percentage of positive tests. All the allergens show a peak of positive reactions during the eighth and ninth years, and again during the thirteenth and fourteenth years.

There were 155 positive reactions for foods. Of these, 21 per cent were for egg, 18 per cent for wheat, 9 per cent for milk and 6 per cent for potato. The four foods just mentioned account for 54 per cent of the 155 positive reactions for foods. For the group of animal emanations there were 257 positive reactions; of these 31 per cent were for cat, 24 per cent for dog, 18 per cent for horse, 15 per cent for chicken feathers and 6 per cent for goose feathers. The pollens gave a total of 256 positive reactions. Of these, 30 per cent were to ragweed, 18 per cent to timothy, 17 per cent to orchard grass, 16 per cent to red top, 7 per cent to cocklebur and 6 per cent to plantain. House dust was frequently found to cause positive reactions.

Of the 300 persons tested, 67 per cent were found reactive to one or more allergens, 47 per cent to animal emanations, 29 per cent to pollens, 25 per cent to foods and 5 per cent to miscellaneous substances. GENGENBACH, Denver.

CONGENITAL LUNG CYSTS. J. D. ADAMSON, Canad. M. A. J. **35**:1 (July) 1936.

Four cases of congenital pulmonary cysts are reported. In forty-nine recent cases described in the literature about twice as many males as females were affected. Cases are discovered at all ages, with percentages as follows: infancy (including the stillborn), 20; first decade, 17; second decade, 10; third decade, 12; fourth decade, 11; fifth decade, 22; sixth decade, 6; seventh decade, 2. Many of the patients have no symptoms; others are stillborn or die of cyanosis and dyspnea immediately after birth. All grades of symptoms may be found, with percentages as follows: dyspnea, 60; cough and expectoration, 44; cyanosis, 22, and hemoptysis, 4. In 16 per cent of the cases the classic symptoms of gross pulmonary sepsis were present. It is believed that pulmonary cysts are congenital for the following reasons: (1) They are quite common in new-born and premature children; (2) they are not infrequently associated with other congenital anomalies; (3) the cells of the cysts are not pigmented; (4) they are common in anomalous and supernumerary lobes or lungs. MOORE, Omaha.

SPONTANEOUS PNEUMOTHORAX. I. H. ALANTAR, Monatschr. f. Kinderh. **65**:235 (April) 1936.

Alantar reports three cases of spontaneous pneumothorax in children aged 3 months, 8 months and 2½ years. In all the condition was a result of tuberculosis with rupture of one or more cavities. He suggests that whenever sudden dyspnea or signs of collapse develop in the course of pneumonia or tuberculosis, this condition should be suspected. The cases ended fatally. GERSTLEY, Chicago.

Diseases of the Gastro-Intestinal Tract, Liver and Peritoneum

THE RELATION IN MAN BETWEEN GASTRIC ACIDITY AND HEIGHT AND WEIGHT. FRANCES R. VANZANT, WALTER C. ALVAREZ and JOSEPH BERKSON, Am. J. Digest. Dis. & Nutrition **3**:83 (April) 1936.

This is a statistical study of the gastric acidity in relation to height and weight, disregarding age.

The essential point in relation to pediatrics is that although the body weight of man increases from twelve to twenty times between birth and maturity, the mean gastric acidity increases only from four to five times.

The differences in gastric acidity observed in men and women of widely divergent build are so small that in ordinary practice an allowance need not be made for them.

MORRISON, Savannah, Ga.

A STUDY OF THE EFFECT OF ANOXEMIA ON THE PYLORIC SPHINCTER IN UNANESTHETIZED DOGS. E. J. VAN LIERE and J. E. THOMAS, Am. J. Digest. Dis. & Nutrition **3**:94 (April) 1936.

The physiologic experiment reported was carried out on unanesthetized dogs. Two dogs had been previously operated on. Each had two abdominal fistulas, one opening into the proximal part of the duodenum and the other opening into the stomach. Rubber tubes were placed in these openings, the two tubes being connected by a collapsible section at the pylorus and attached to a pressure tonometer and a recording device. The dogs were then made to breathe from a rubber bag oxygen in mixtures of 6, 9 and 14 per cent, and the tone and contractions of both the pyloric sphincter and the pyloric antrum were recorded.

In all degrees of anoxemia the tone of the pyloric sphincter was increased, and the tone of the gastric musculature (antrum) was depressed, the intensity varying proportionately to the amount of anoxemia produced.

These combined factors may be sufficient to account for the delayed gastric emptying time seen in anoxemia.

MORRISON, Savannah, Ga.

VON GIERKE'S GLYCOGEN DISEASE. LIONEL M. LINDSAY, ALAN ROSS and F. W. WIGGLESWORTH, Ann. Int. Med. **9**:274 (Sept.) 1935.

A case of von Gierke's disease of the hepatic type, occurring in a boy aged 27 months, is reported. The etiology and pathogenesis are discussed briefly. The diagnosis was made from clinical and biochemical observations and confirmed by biopsy of a section of hepatic tissue.

The effect of epinephrine on the values for the sugar content and the lactic acid content of the blood is shown. In addition, the values for the blood sugar levels during fasting and following the oral ingestion of dextrose are recorded.

Death occurred subsequent to this report. The liver was found to weigh 2,150 Gm. The complete pathologic report will be published at a later date.

READING, Galveston, Texas.

GRANULOMA PYOGENICUM OF THE TONGUE. RICHARD J. KELLY, Arch. Dermat. & Syph. **31**:864 (June) 1935.

In a girl 13 years old a lesion the size of a pea developed on the circumvallate papillae within thirteen days. The lesion was reddish gray and was "slightly compressible, ending in a raised, annular and firm base (the hernia ring formation often seen with granuloma pyogenicum)." It was removed by electrocoagulation and curettement under anesthesia with procaine hydrochloride.

DULIN, Iowa City.

Ulcerative Typhlitis Simulating Acute Appendicitis; Report of Case. Leo M. Zimmerman and Richard E. Heller, Arch. Pediat. **52**:712 (Oct.) 1935.

A case of ulcerative typhlitis is described, the clinical features of which closely simulated those of acute appendicitis. The cecitis was apparently secondary to acute pharyngitis.

Waddell Jr., University, Va.

Pneumococcus Peritonitis. H. Rappaport and Michael A. Brescia, Arch. Pediat. **52**:766 (Nov.) 1935.

A case of pneumococcic peritonitis with recovery is reported, with a brief discussion of the literature for the last twenty years. The favorable result is attributed to the use of large amounts of serum and repeated blood transfusion.

Waddell Jr., University, Va.

Inguinal Hernia as a Cause of Pylorospasm in Infancy. Julian L. Rogatz, Arch. Pediat. **52**:778 (Nov.) 1935.

A case of prolonged vomiting of a projectile nature in an 8 month old baby was relieved promptly by correction of bilateral inguinal hernia.

Waddell Jr., University, Va.

Pharyngogenic Hematogenous Streptococcic Peritonitis. Joseph Felsen and A. G. Osofsky, Arch. Surg. **31**:437 (Sept.) 1935.

Pharyngogenic hematogenous streptococcic peritonitis is a metastatic inflammatory lesion of the peritoneum caused by a streptococcic hematogenous invasion from a primary focus in the tonsils and pharynx. The disease is characterized by an abrupt onset during or after the subsidence of any infection in the throat. In all the eight cases reported there was a definite antecedent history of sore throat. The average period that elapsed between the angina and the onset of acute abdominal symptoms was six days. The average period of survival was four and seven-tenths days, and the mortality was 100 per cent. Felsen and Osofsky reproduced the disease in rabbits by the intravenous injection of broth cultures containing strains recovered from their patients. This was done to study the mechanism of peritoneal involvement. As the organisms injected intravenously in the rabbits were recovered in the feces, it was assumed that they are brought to the intestines in the blood stream and then excreted through the intestinal wall into the lumen of the intestine. The organisms in the intestine pass out through the focal lesions into the peritoneal cavity, and peritonitis is established.

Kaiser, Rochester, N. Y.

Acute Appendicitis and Associated Lesions. Rudolph N. Schullinger, Arch. Surg. **32**:65 (Jan.) 1936.

Schullinger has added some valuable facts to the large amount of statistical information on the mortality from acute appendicitis. In order to determine under what conditions the mortality was influenced the cases of appendicitis were grouped under the following classifications: acute appendicitis, acute appendicitis with acute local peritonitis, acute appendicitis with peritoneal abscess, acute appendicitis with acute diffuse peritonitis and acute appendicitis with progressive fibrinopurulent peritonitis. The data were collected at the Presbyterian Hospital in New York and covered an eighteen year period. It was found that the general mortality from acute appendicitis and its associated lesions had definitely declined. When the mortality for the separate groups was studied, the decline was not found the same for all groups. The death rate for simple acute appendicitis remained at a

constantly low level. That for acute appendicitis with acute local peritonitis showed a distinct decline. On the other hand, in the group in which there was peritoneal abscess and in the group in which there was acute diffuse peritonitis, the rate increased. The mortality remained consistently high in the fifth group. An analysis of the deaths and a discussion of certain means of preoperative, operative and postoperative preventive measures are presented for each group. The measures advocated for prevention are described and may be a factor in eventually reducing the mortality in this disease. KAISER, Rochester, N. Y.

SHOCK: THE MECHANISM OF DEATH FOLLOWING INTESTINAL OBSTRUCTION. V. H. MOON and D. R. MORGAN, Arch. Surg. **32**:776 (May) 1936.

Moon and Morgan reviewed the literature on the mechanism by which death results from intestinal obstruction. In spite of extensive experimentation there has been no agreement as to the causes of death. Though it had been assumed that shock was responsible for death in intestinal obstruction, no characteristic changes had been demonstrated at necropsies. The authors produced intestinal obstruction in dogs and studied the gross and microscopic visceral changes post mortem. They found these changes identical with those which accompany shock produced by various means. These changes are: marked distention and engorgement of the capillaries and venules in the viscera; edema and ecchymoses of the lungs and gastro-intestinal mucosae, and effusions into serous cavities. From the results of these experiments they assume that intestinal obstruction is one of the many conditions which will produce characteristically the shock syndrome.

KAISER, Rochester, N. Y.

CLINICAL STUDY UNDER CONTROLLED CONDITIONS OF 1,083 CHILDREN WITH HOOKWORM. A. E. KELLER, J. T. GOOGE, H. B. COTTRELL, D. G. MILLER JR. and R. H. HARVEY, J. A. M. A. **105**:1670 (Nov. 23) 1935.

The stools of 79.5 per cent of 1,083 children studied were infested with eggs of hookworm. Of this group, 62.2 per cent had a light infestation, and 17.3 per cent had a moderate or heavy worm burden.

When the level of infestation reached approximately 100 or more hookworms a larger percentage of children complained of symptoms, and the degree of dyspnea, weakness and fatigue, and edema was increased.

There was only a slight variation in the degree of underweight in the infested groups as compared with the controls, and no striking differences were noted in the incidence of anemia and malnutrition between the control group and the group with light infestation. The patients with the heaviest worm burdens had the greatest degree of anemia and malnutrition. The number of eosinophils was increased in all the groups (averaging 9.6 per cent in the controls), but for these known to have hookworms the number was greater (from 11.9 to 17.9 per cent). No relationship between the percentage of eosinophils and the number of hookworms could be determined, and in groups with hookworm from 4.3 to 17 per cent had eosinophil counts of less than 5 per cent. Removal of hookworms alone will bring about only partial and temporary improvement in the health of children, for both the control group and the infested groups showed malnutrition and anemia and received improperly balanced diets. BONAR, Salt Lake City.

ORAL LESIONS DUE TO HYPERSENSITIVENESS. VIRGIL LOEB, J. Am. Dent. A. **22**:2063 (Dec.) 1935.

Loeb discusses briefly lesions in the mouth due to hypersensitiveness and idiosyncrasy. There is mention of angioneurotic edema, an urticarial unilateral swelling of the tongue and an idiosyncratic reaction of the mucous membrane in the mouth to drugs contained in the common laxatives and sedatives. NOYES, Chicago.

CONGENITAL PYLORIC OBSTRUCTION. CHESTER F. MCGILL, New England J. Med. **213**:567 (Sept. 19) 1935.

This is an interesting résumé of the historical literature on congenital pyloric obstruction, starting with the earliest reference to this condition by George Armstrong in England in 1777. The case reported was the third one of a similar condition in the same family. All three patients died. Then follows the earliest reference in America, in which Hezekiah Beardsley of Connecticut in 1787 described in interesting detail the clinical and postmortem observations on a 5 year old child with symptoms dating from infancy. Recent research studies on the causation and medical treatment of the condition are described.

McGill believes that in the present status of the knowledge concerning the problem, medical management should first be tried, with the curve for weight, determination of the amount of fecal matter in each twenty-four hours and the general condition of the patient, as stated by Sauer, taken as the criteria for determining how long the treatment should be continued. Medical treatment may be followed by the Fredet-Rammstedt pyloromyotomy, if necessary.

GENGENBACH, Denver.

GIANT DIVERTICULA OR REDUPLICATIONS OF THE INTESTINAL TRACT. HENRY W. HUDSON JR., New England J. Med. **213**:1123 (Dec. 5) 1935.

These cases of giant diverticula or reduplication of the intestine are reported with considerable detail. The first patient was operated on twice (at 3 and 6 months of age), with marked improvement, but died on the operating table during a third operation at the age of 2 years. Starting about 2 feet (60 cm.) above the ileocecal valve, the diverticulum ran distally parallel to the ileum and within the leaves of the mesentery, toward the ileocecal valve, for about 16 inches (40 cm.). No point of communication with the ileum was demonstrated.

The second patient was operated on at 6 months of age and died twelve hours later. The diagnosis was: jejunum of the duplex type, with the gastric mucosa showing acute and chronic ulceration. There was no communication between the jejunum and the diverticulum. Sections through the dimpled areas where the two structures were adjacent showed a double muscular wall with a slight amount of intervening fibrous tissue.

The third patient, aged 12 years, also died after an emergency operation for intestinal obstruction. The volvulus involved about 4 feet (122 cm.) of the lower part of the ileum and had rotated clockwise about 80 degrees. The ileum was edematous but not greatly distended. Within the mesentery, parallel and intimately opposed to the mesenteric edge of the ileum, was a reduplication of the bowel for a distance of about 4 feet. Near its proximal end was a large perforation about 1½ inches (4 cm.) in diameter, from which a small amount of bright blood escaped.

The theories advanced in explanation of the development of these anomalies are summarized. A bibliography of the literature on enteric cysts, diverticula and reduplications of the intestinal tract is also presented.

GENGENBACH, Denver.

MESENTERIC CYST. L. G. LIVINGSTON, South. M. J. **28**:1028 (Nov.) 1935.

Embryonal rests, trauma and a malignant condition probably account for the majority of mesenteric cysts and tumors. The condition reported by Livingston probably was an embryonal rest cyst, with gradual enlargement and bleeding into the cyst. Beginning intestinal obstruction, due to stretching of the intestinal wall, made surgical intervention imperative.

SCHLUTZ, Chicago.

CONGENITAL PYLORIC STENOSIS WITH OBSERVATIONS BASED ON 209 CONSECUTIVE CASES. W. A. THOMPSON and WILFRID GAISFORD, Brit. M. J. **2**:1037 (Nov. 30) 1935.

The experience of the authors with congenital pyloric stenosis is outlined. The discussion is along more or less conventional lines.

ROYSTER, University, Va.

POST-OPERATIVE TREATMENT OF CONGENITAL PYLORIC STENOSIS. ROBERT RUTHERFORD, Brit. M. J, **2**:1101 (Dec. 7) 1935.

A case of congenital pyloric stenosis is reported, with an account of the operation. Immediately after the operation the child was removed from the nursing home to its own home because Rutherford thinks that hospitalization in these cases is inadvisable and that the child with this condition needs personal nursing.

ROYSTER, University, Va.

COELIAC DISEASE. FRED SHIPPMAN, Canad. M. A. J. **34**:243 (March) 1936.

This is an excellent review of the subject of celiac disease, with a detailed report of three cases. The important points stressed in the diagnosis are: (1) loose stools containing more than 2 Gm. of fat and the absence of any infection to account for the diarrhea; (2) physical findings, such as a protuberant abdomen, marked gluteal atrophy, general wasting, hyperchromic or hypochromic anemia and changed disposition, (3) lowering of the sugar tolerance (when a mixture of dextrose and levulose was used the sugar tolerance curve was normal).

In treatment skim protein milk is used in the beginning, and fat-free broth, white of egg, curds made of skimmed milk, and white meat of chicken are gradually added. As the condition improves, carbohydrate is added in the form of bananas. Zwieback is then added, and later other carbohydrates, such as well cooked cereal and rice, are given. Vitamins A and D are essential in the diet. Vitamin B, given in the form of marmite, improves the appetite and prevents the onset of anemia. Orange juice is given to supply vitamin C.

The prognosis is good in most cases. A careful follow-up study should be made in all cases.

MOORE, Omaha.

THE TREATMENT OF FAMILIAL ACHOLURIC JAUNDICE. S. O. COWEN, M. J. Australia **1**:265 (Feb. 22) 1936.

The results of splenectomy in twenty of thirty-three personally observed patients suffering from familiar acholuric jaundice bear out the generally accepted view that the operation brings about complete and lasting freedom from symptoms. The jaundice disappears almost immediately, and the anemia improves so rapidly that within six weeks a bedridden child may be well enough to return to school. Because of the dramatic nature of the improvement, preoperative transfusion is seldom needed, and splenectomy may be undertaken without hesitation even in a patient who appears almost desperately ill. In Cowen's series of twenty cases there has been no operative mortality, and the operative morbidity has been negligible.

It is not sufficiently recognized that, generally speaking, the disease follows much the same course in the individual members of each affected family. To illustrate this point that variations in severity are familial rather than individual, two family histories are cited. The family history, then, as well as the clinical findings in the individual patient, should be considered in determining the advisability of splenectomy.

When biliary pigment stones are present, as in seven of the twenty patients concerned in this report, the gallbladder should be emptied by crushing the stones digitally or by cholecystotomy. Cholecystectomy should be performed only when evidence of cholecystitis is present.

GONCE, Madison, Wis.

DIAGNOSIS AND TREATMENT OF ACUTE ABDOMINAL CONDITIONS IN CHILDREN. LANCELOT E. BARRINGTON-WARD, Tr. Med.-Chir. Soc. Edinburgh, 1936, p. 25; in Edinburgh M. J. **47**:25 (March) 1936.

This paper deals with the abdominal emergencies in the Great Ormond Street Hospital for the previous five years, the cases numbering two hundred and eighty-seven. In order of frequency, appendicitis was present in 41.8 per cent and intussusception in 37.6 per cent (such a large number being due to the attraction of a children's hospital for this condition rather than indicating the frequency in general practice). Cases of intestinal obstruction and peritonitis of the streptococcic or of the pneumococcic type each formed 7.7 per cent of the total number.

Barrington-Ward appreciates the pitfalls of an early diagnosis, such as determining whether the abdominal symptoms really arise from the abdomen. Tonsillitis can cause characteristic symptoms; in tuberculous meningitis there may be a hard, retracted, painful abdomen at the onset; pleurisy near the base of the right lung simulates appendicitis; the symptoms of disorders of the urinary tract may mimic those of abdominal surgical conditions, because of pyelitis, while calculus of the kidney and ureter and malformations of the kidney and ureter, such as double kidney and double ureter, may produce symptoms in the abdomen. However, in all the aforementioned conditions there should be localizing signs for the particular primary lesion. The throat, chest, and urine should be examined in every case of abdominal pain. In such instances of extra-abdominal lesions the abdominal signs are not clear (the author states that the physical signs are "out of step"). The age of the child may help decide the diagnosis, and, with the exception of intussusception, every child with a true surgical disease has either obstruction or inflammation—which one it is must be decided. This decision will depend on the character of the pain, on the presence of tenderness and on the existence of voluntary or involuntary rigidity.

The author next discusses the general treatment of the so-called "acute abdomen," emphasizing special points in the diagnosis of the aforementioned conditions.

He mentions briefly the following rarities: Meckel's diverticulum, acute cholecystitis, perforated duodenal ulcer and torsion of the ovary.

NEFF, Kansas City, Mo.

ETIOLOGY AND PATHOGENESIS OF PERIODIC VOMITING ASSOCIATED WITH ACETONEMIA. A. B. MARFAN, Arch. de méd. d. enf. **39**:5 (Jan.) 1936.

Following a discussion of the characteristic features of periodic vomiting associated with acetonemia, Marfan gives extended consideration to the present day views concerning the etiology. As a disorder peculiar to young children and more common among boys than girls, cyclic vomiting has become a controversial subject. It is asserted that almost without exception these children are victims of a particular constitution or habit, which is known in France as the arthritic or neuro-arthritic diathesis. Marfan feels this term is badly chosen and suggests that among the conditions favoring the development of acetonemia with vomiting it will be necessary to consider a group entirely apart from those of a manifestly allergic or anaphylactic origin.

Careful inquiry usually elicits a striking tendency to neuro-arthritism and a disposition to myalgia, neuralgia, gout, migraine, asthma, eczema, lithiasis and obesity in the immediate family of these patients or in the collateral branches. The children themselves may be subject to prurigo, urticaria and attacks of asthma which alternate with the crises of vomiting. Hutinel reported such a case in a boy of 6 years.

At the age of puberty, migraine, cholemia, hepatic colic or diabetes may appear. It is fair to assume that such a hereditary taint creates in certain persons a particularly unstable chemical equilibrium in the fluids and tissues of the body, which leads to metabolic errors that constitute the cause of periodic vomiting.

Marfan notes that while provocative causes of a crisis may appear spontaneously and suddenly, there is usually some minor disturbance of the health, due to such factors as the eruption of a tooth, mental exhaustion, emotional shock, an excess of fat in the diet, constipation, the administration of a laxative (especially mild mercurous chloride), surgical anesthesia, lumbar puncture, minor injuries or the onset of an eruptive fever.

These observations embrace all the items usually considered in the etiology of recurrent vomiting associated with acetonemia. Holt's views concerning the rôle of a diet habitually rich in fats are disputed, as are also the conclusions of other authors who attribute this syndrome to gastro-intestinal disease, enteroptosis, aerophagia, appendicitis and duodenal stenosis.

AMESSE, Denver.

PYLORODUODENAL STENOSES IN NURSLINGS. G. PAISSEAU, E. BŒGNER and C. VAILLE, Arch. de méd. d. enf. **39**:27 (Jan.) 1936.

There are exceptional forms of pyloric stenosis which are not readily identified by the usual methods but in which a diagnosis is made relatively easy through the manifestations of what the authors term "a humoral syndrome." American clinicians have demonstrated a high degree of hypochloremia in occlusion of the digestive tube among adults; there is a coincident rise of the alkaline reserve. Certain French investigators have established the existence of similar chloropenia in stenosis of the pylorus in infants and have emphasized its value in diagnosis, contrasting it with the hypochloremia accompanied by a marked lowering of the alkaline reserve that was noted by Ribadeau-Dumas and others in the choleriform syndrome with vomiting seen during the early months of life. This phenomenon may also aid in differentiating the vomiting in which alkalosis and the reduction of chlorides do not appear.

Treatment of this condition, based on such a hypothesis, is no less important. In cases of intestinal obstruction in adults the efficacy of hypertonic solution of sodium chloride administered by injection has been clearly proved. In four cases of pyloric stenosis of nurslings, reported by the writers, hypochloremia and alkalosis were successfully combated by intravenous injections of a 20 per cent solution, in doses of from 3 to 5 cc., or intrarectal injections of 20 cc. Two of the cases observed were of the classic type, while the remaining two were concerned with stenosis of the duodenum. It is pointed out that this treatment is simply an adjuvant to the necessary surgical procedures long established.

AMESSE, Denver.

PNEUMOCOCCIC PERITONITIS. J. P. GRINDA, Gaz. d. hôp. **108**:1397 (Oct. 16) 1935.

Four children and a young adult were operated on because of a condition that had been diagnosed as appendicitis. Only one died, on whom operation was performed on the eighth day of the disease. Grinda emphasizes that none of these patients showed rigidity of the abdominal wall, except in the terminal stage. Local pain was less marked in these cases of pneumococcic peritonitis than in cases of appendicitis, while the general condition seemed worse. All the patients had severe bronchopneumonia after the operation, which the author attributes to the fact that general anesthesia was used. He suggests the use of local anesthesia and feels that the operation is advisable.

KAJDI, Baltimore.

VOMITING FROM AEROPHAGIA IN THE INFANT UNDER SIX MONTHS. P. LEREBOULLET, MARCEL LELONG and P. AIMÉ, Presse méd. **43**:1541 (Oct. 5) 1935.

Vomiting from aerophagia in infants is an example of trouble arising not from pathologic changes but from the highly specialized physiologic condition of children of this age, specifically, from the mechanism of the deglutition of liquids. Since the amount of air swallowed with liquids is far greater than that swallowed with solids, distention of the stomach produces in certain infants a type of habitual

vomiting which disappears when semisolid food is given. The vomiting begins soon after birth, without the initial latent phase characteristic of pyloric stenosis. It is to be differentiated from vomiting due to starvation, vomiting from incorrect feeding and vomiting caused by obstruction. The infants are usually healthy, gluttonous babies who show no signs of any other disturbance. The fact that they take their feedings ravenously apparently is a large factor in the mechanics of the disorder, as a slow distention is unlikely to have the same effect. Numerous roentgenograms are presented showing the effect of swallowing large quantities of air. Three solutions are offered for the problem: (1) feeding by tube, (2) increasing the consistency of the food by using evaporated milk or cereal, and (3) postural evacuation of the air by holding the infant upright immediately after feeding, then placing him on the left side to allow the bubble to pass through the pylorus and finally, just before the next feeding, turning him on the right side to bring any remaining food in contact with the pylorus.

BIEKER, St. Petersburg, Fla.

ACUTE APPENDICITIS. RAOUL CHARLES MONOD, Rev. méd.-sociale de l'enf. **4**:81 (March-April) 1936.

Monod gives a brief discussion of the symptoms and course of acute appendicitis, which he says is much more frequent in children than in adults. He gives the differential diagnosis of pneumonia, pneumococcic peritonitis and typhoid.

BROWNE, Detroit.

PRANDIAL DIARRHEA IN THE INFANT. R. M. CALZADA RODRÍGUEZ, Arch. españ. de pediat. **20**:212 (April) 1936.

Prandial diarrhea is a variety of constitutional diarrhea, the essential character of which is the discharge of diarrheal stools at the moment of taking or immediately after taking food. Infants subject to it usually show signs of exudative or neuropathic diathesis. Anaphylaxis or food sensibility does not play any important part in the pathogenesis. Infection is not a primary cause and does not influence the subsequent course. The author believes that exaggeration of the gastrocolic reflex is the chief mechanism in the production of this form of diarrhea. The nutritional state is often affected by it.

Three factors condition it—constitutional anomalies, the type of food given, and intercurrent infections. The extent to which these factors operate influences the prognosis. The hereditary factor may also enter.

This form of diarrhea is generally very resistant to dietetic and medicinal measures. Remedies which affect or inhibit action of the vagi seem to be most effectual.

SCHLUTZ, Chicago.

HEPATIC ABSCESS IN A FOURTEEN MONTH OLD CHILD. A. CARBONELL Y SALAZAR and B. SÁNCHEZ SANTIAGO, Arch. de med. inf. **5**:143 (June) 1936.

Following a gastro-intestinal upset a 14 month old girl presented a fluctuating tumor the size of an egg at the base of the thorax on the right, in the axillary midline. Puncture showed a gram-negative bacillus and a gram-positive diplococcus. The treatment, which resulted in cure, was the daily injection of antiperitonitic serum and emetine hydrochloride.

SANFORD, Chicago.

ATROPHIC CIRRHOSIS IN A CHILD AGED SEVEN YEARS. HECTOR MORIGÁN, Arch. de pediat. d. Uruguay **7**:76 (Feb.) 1936.

A child showed marked icterus and a large liver at the age of 3 years. The icterus persisted over one year, then entirely disappeared. After an interval of two years of good health, severe hepatic insufficiency developed suddenly and rapidly led to a fatal termination. At autopsy the liver showed the characteristic picture of the cirrhosis of Laënnec.

SCHLUTZ, Chicago.

THE PATHOLOGY OF ILEOCOLITIS. AUGUSTIN CASTELLANOS, Bol. Soc. cubana de pediat. **8**:258 (May) 1936.

Intense infiltration of lymph follicles characterizes ileocolitis in infancy. The infantile type differs from the adult type in this respect.

In infants under 1 year of age intense inflammation of the submucosa is found. Ulcerated lesions and edema of the submucosa are often observed in the lower part of the colon and in the region of the sigmoid flexure.

Castellanos is of the opinion that the adenolymphoid tissue of the intestine plays an important rôle in the defense against infection with the dysentery bacillus.

SCHLUTZ, Chicago.

ENTEROCOLITIS AND DYSENTERY IN INFANCY IN JUIZ DE FORA. OLAVO LUSTOSA, J. de pediat., Rio de Janeiro **3**:193 (May) 1936.

Lustosa reviews the subject of dysentery, and states the belief that there is a more specific infection than is usually thought. Occasionally the colon bacillus can become pathogenic. Since the use of blood transfusions and supporting treatment the mortality from this condition in Juiz de Fora has been greatly lessened.

SANFORD, Chicago.

EMACIATION AND LOW BASAL METABOLISM RESULTING FROM CARDIOSPASM. LOTTE HOTOP, Monatschr. f. Kinderh. **63**:409, 1935.

A 10 year old girl was brought to the clinic because of extreme emaciation and daily vomiting, and the basal metabolic rate was minus 43. Roentgenograms confirmed the diagnosis of cardiospasm. After using a surprising number of proprietary remedies, the author resorted to dilation, which resulted in improvement.

GERSTLEY, Chicago.

MIGRATION OF ROUND-WORMS THROUGH THE NORMAL INTESTINE. W. POTTER, München. med. Wchnschr. **82**:1640 (Oct. 11) 1935.

A 3 year old boy died with symptoms of peritonitis. At autopsy there was generalized purulent fibrinous peritonitis. Two round-worms were observed in the peritoneal cavity. The jejunum and ileum contained about two hundred parasites. A perforation was found in the lower part of the jejunum.

BRAHDY, Mount Vernon, N. Y.

REPORT OF A CASE OF HEMIGLOSSITIS PHLEGMANOSA IN AN INFANT. JAN KOSSAKOWSKI, Pedjatrja polska **15**:120, 1935.

The important point about hemiglossitis phlegmanosa is its rare occurrence. This infection, particularly as evidenced by any abrasions on the tongue and by debility of the infant, is local or constitutional. The prognosis of suppuration of the tongue is bad unless the condition is recognized and surgical intervention is instituted early.

KRUPINSKI, Chicago.

THE ETIOLOGY OF PYLOROSPASM (HYPERTROPHIC STENOSIS OF THE PYLORUS, HIRSCHSPRUNG). T. HALBERTSMA, Acta pædiat. **18**:463, 1936.

Halbertsma advances the thesis that the fundamental feature of the pathogenesis of hypertrophic stenosis of the pylorus is elongation of the pyloric canal. This anatomic abnormality constitutes a relative obstruction of the outlet of the stomach; the obstruction, in turn, produces spasm and consequent hypertrophy of the pyloric sphincter. The clinical observations on which the assertion is based are

above criticism; whether or not they support the author's claim must be left to the reader to judge. Few will deny that hypertrophic pyloric stenosis is a congenital, sometimes a familial, anomaly. The paper contains reports of a number of familial cases which the author has observed personally, together with a brief survey of previous descriptions of the occurrence of more than one case in the same family.

McCune, New York.

Acute Atrophy of the Liver and Catarrhal Jaundice in a Brother and Sister. C. Hirschberger, Acta pædiat. **18**:482, 1936.

Since 1918 the mounting incidence of hepatogenous jaundice has stimulated widespread attention, resulting in a large number of explanatory hypotheses. In view of the increased vulnerability of undernourished liver cells it is within the realm of possibility that the increase may be related to the impoverished diet on which many persons have been compelled to live during the world economic crisis. However, the frequent appearance of jaundice in epidemic form attests to the presence of infectional factors behind the increase. The precise nature of the infecting agent and the route along which it travels are still unknown. Purely for purposes of convenience the terms "catarrhal jaundice" and "simple jaundice" have been adopted to designate the disease. In view of the diffuse nature of the cholangeitis and hepatitis which accompany the infection it is rather surprising that the liver cells so rarely suffer permanent damage and that the prognosis is so uniformly good. Although several large epidemics have been reported in as many countries, only a small number of reports of cases in which acute atrophy occurred have been published. Uncommon as this complication is in adults, it is even more rare among children.

Hirschberger reports the case of a 7 year old girl who fell ill during a small local epidemic of catarrhal jaundice and died during the fourth week of illness; she presented the well known clinical features of acute yellow atrophy, including the presence of crystals of leucine and tyrosine in the urine. The diagnosis was confirmed at autopsy. Her 11 year old brother fell victim to the same infection on the day the girl died. Although jaundice was intense, his illness was mild and terminated with recovery in three weeks. The following questions are proposed: Why does acute atrophy of the liver select the female sex so predominantly? Why, when catarrhal jaundice is usually so harmless a disease, does it occasionally lead to fatal atrophy of the liver? The questions are not answered.

McCune, New York.

Nervous Diseases

On the Differentiation of Colored Cerebrospinal Fluids. F. H. Robinson and B. N. Miller, Am. J. M. Sc. **191**:538 (April) 1936.

In this study of colored spinal fluids Robinson and Miller attempt to explain the mode of production of such fluids and to suggest a routine use of the benzidine test in their etiologic differentiation.

Briefly, the benzidine reaction is positive in cerebrospinal fluid containing a hemoglobin dilution of 1:50,000 (100 erythrocytes per cubic millimeter) but not in one containing a dilution of 1:100,000 (50 erythrocytes per cubic millimeter); the benzidine reaction in the supernatant fluid obtained after centrifugation at high speed is of value in differentiating hemorrhage into the cerebrospinal fluid at the time of puncture from subarachnoid hemorrhage; an extramedullary tumor compressing the spinal cord in its growth has been reproduced experimentally in dogs, with a resulting Nonne-Froin syndrome in the cerebrospinal fluid below the level of the compression; the yellow spinal fluid characteristic of cord compression gives a negative benzidine reaction.

Henske, Omaha.

FEVER THERAPY IN CHOREA AND IN RHEUMATIC CARDITIS WITH AND WITHOUT CHOREA. LUCY PORTER SUTTON and KATHARINE G. DODGE, J. Lab. & Clin. Med. **21**:619 (March) 1936.

The most satisfactory treatment of chorea is fever therapy, by whatever means produced. The presence of carditis is not a contraindication to this type of therapy. In fact, the authors feel that subacute rheumatic carditis may be definitely benefited by fever therapy.

McMURRAY, Galveston, Texas.

CONGENITAL CEREBELLAR ATAXIA. R. S. FREW, Proc. Roy. Soc. Med. **29**:211 (Jan.) 1936.

A boy of 8 years did not sit up until he was 3 years old and had never walked well. At 3 weeks of age a Rammstedt operation had been performed for pyloric stenosis. On examination it was noticed that there were athetoid movements of the trunk, face and limbs. The speech was explosive in type. There were general muscular hypotonia and ataxia of both arms and legs. The gait was ataxic, and the child fell frequently. Mentally he was bright and intelligent.

WILLIAMSON, New Orleans.

THE SYNDROME OF DYSTONIA OF TORSION. JULES R. DREYFUS, Arch. de méd. d. enf. **39**:149 (March) 1936.

Although this syndrome is relatively rare, Dreyfus has been privileged to study three cases. He reports the histories and clinical findings in detail.

Three types of pathogenesis are described: (1) idiopathic or cryptogenic, (2) postoperative or hemorrhagic and (3) symptomatically resembling Wilson's disease.

In the first case reported the patient, a boy of 13, presented the early signs of torsion several weeks after a severe fright, which was followed by a chill. The second case concerned a boy of 6 who suffered from frequent attacks of nasal hemorrhage. The adenoids were removed, and dystonia developed the following day, which Dreyfus ascribes to cerebral hemorrhage, probably in the region of the corpus striatum. This case conformed to the type described by Glanzmann, who considered the source as thrombasthenia. The third patient observed, a boy at the Children's Hospital, Bern, Switzerland, manifested symptoms of progressive lenticular degeneration with cirrhosis of the liver, strongly resembling the so-called disease of Wilson.

Autopsies in similar cases have not thrown much light on the origin of this peculiar dystonia, but enough has been found to justify the suspicion that in most instances the corpus striatum, the center of coordination, is seriously involved and antagonistic action of the muscles thus permitted.

AMESSE, Denver.

THE MENTAL STATE AFTER ATTACKS OF CHOREA. M. SCHACHTER, Progrès méd., June 26, 1936, p. 949.

Schachter reports three cases in which mental instability developed after attacks of chorea. The discussion which follows is largely speculative, dealing with constitution as a predisposing factor in the development of chorea and also with the possible action of the infective virus on the areas of the brain which have to do with the emotions.

LESLIE, Evanston, Ill.

IS CHOREA AN AVITAMINOSIS? VICENTE BAPTISTA, J. de pediat., Rio de Janeiro **3**:127 (March) 1936.

Hidenbauer's treatment of four patients with chorea with a vitamin B preparation is discussed.

SANFORD, Chicago.

MENINGEAL MESENCHYMOMA OF FOREIGN BODY ORIGIN. O. MARBURG, Virchows Arch. f. path. Anat. **294**:759, 1935.

A boy aged 15 years was operated on for the removal of an astroblastoma of the parietal lobe. Hemorrhage at the time of operation necessitated packing of the wound. After recovery jacksonian seizures continued, and headache returned and became progressively worse. Five years after the first operation the patient was again operated on. At the site of the first operation there was found a firm tumor of the leptomeninges that invaded the brain and could not be completely removed. The tumor contained a strip of iodoform gauze left from the first operation. Death was due to meningitis. The tumor was cellular and anaplastic, and its cells were polymorphic, with a predominance of cells of the young spindle type. Marburg discusses the relation of the tumor to the foreign body and the morphology and possible origin of tumors arising in the meninges. For such tumors the designation "meningeal mesenchymoma" or "primitive meningoblastoma" may be used, but only in a descriptive sense, since such tumors may be of mesectodermal origin. SCHULTZ, Evanston, Ill. [ARCH. PATH.]

QUANTITATIVE ESTIMATION OF THE BOUND SUGAR CONTENT IN SPINAL FLUID IN MENINGITIDES OF CHILDREN. Y. YAMASAKI, J. Pediat. (Tokyo), no. 430, Feb. 20, 1936, p. 364.

Using the micromethod of Iizuka for bound sugar and that of Hagedorn and Jensen for free sugar, Yamasaki made the following observations:

1. In normal cerebrospinal fluid the bound sugar has an average value of 0.001 Gm., and the free sugar, of 0.061 Gm., per hundred cubic centimeters.

2. In lead encephalopathy the spinal fluid contains, on the average, 0.005 Gm. of bound sugar and 0.077 Gm. free sugar per hundred cubic centimeters.

3. In tuberculous meningitis the values for bound and free sugar are 0.005 Gm. and 0.031 Gm. per hundred cubic centimeters, respectively.

4. In epidemic meningitis the average value of bound sugar is 0.009 Gm. and that of free sugar 0.017 Gm. per hundred cubic centimeters. A tendency for decrease in bound sugar and increase in free sugar makes for a good prognosis.

5. In pyogenic meningitis the values for both bound and free sugar approximate those in epidemic meningitis.

6. In various diseases of the central nervous system other than meningitis, the free sugar is increased during convulsions but is otherwise normal.

KATO, Chicago.

Psychology and Psychiatry

COMMON SENSE IN REARING CHILDREN FOR LIFE. IRA S. WILE, Arch. Pediat. **52**:749 (Nov.) 1935.

The author defines as common sense "what would be regarded as the ordinary sense or the locally prevalent sense based upon a feeling of logicality with its slight modification by intelligence. Such sense cannot be unusual in nature or beyond the customary levels of unguided thinking." It is believed that little of the progress made so far in child welfare can be laid at the door of common sense, and the main tenor of the article is in accord with this statement.

WADDELL JR., University, Va.

THE RELATIONSHIP OF THE FLAT CHEST TO INTELLIGENCE. S. A. WEISMAN, Ann. Int. Med. **9**:451 (Oct.) 1935.

Previous observations by the author that the chest of the healthy normal adult is flat and that children from better environments not only are taller and heavier

but have chests of the flat type prompted this study to determine the relationship of the shape of the chest to intelligence.

The material consisted of 14,844 Minneapolis school children between the ages of 5 and 7. The number of boys and the number of girls were approximately equal. Intelligence was determined by the grades the children received in their school work. The pupils were grouped on the basis of their grades, and the average thoracic index was determined for each group according to age.

The conclusion was reached that the flat-chested children are, on the average, taller and heavier and display a higher degree of intelligence than the deep-chested children.

READING, Galveston, Texas.

LEFT-HANDEDNESS. JOSEPH J. MICHAELS and SYLVIA E. GOODMAN, Arch. Neurol. & Psychiat. **34**:758 (Oct.) 1935.

A statistical study of four hundred and seventy-five normal children at camp is reported. A negative, but insignificant, correlation was found between left-handedness and the presence of enuresis, tantrums of temper, disturbances of sleep, dreaming and failures in school. A slight positive association was found between left-handedness and the presence of impediments of speech, thumb-sucking, nail-biting, the Chvostek sign and a family history of left-handedness.

BEVERLY, Chicago.

THE MANAGEMENT OF NEGATIVISM IN YOUNG CHILDREN. R. L. JENKINS, M. Rec. **142**:507 (Dec. 4) 1935.

The term negativism is used for a tendency to oppose the normal physiologic desires and to denote a propensity to do the opposite of what is directed. This is frequent in young children. It tends spontaneously to disappear unless reenforced by bad management. A program of management must be based on an estimate of the total situation of the child. As a general method of meeting the problem, punishment or any other "frontal attack" is contraindicated. In general, ignoring the behavior is perhaps the most useful course to take, especially when this is accompanied by liberal praise and recognition of positive accomplishments. Reduction in the amount of attention given the child should be postponed until after the negativism is under control. When negativism is related to an essentially morbid relationship between the parent and the child it usually cannot be remedied except by modification of such relations. The article is accompanied by reports of three cases.

WILLIAMSON, New Orleans.

THE MENACE OF NERVOUS AND MENTAL FATIGUE IN SCHOOL CHILDREN. N. P. BROOKS, M. Rec. **142**:512 (Dec. 4) 1935.

Alcoholism, syphilis, consanguinity and hereditary disorders are no more prevalent in the United States than in other countries, yet cases of nervous and mental disturbance are far more common. The author believes that the basis of this is to be found in the overworked school child. If Young's formula is applied to the work a child should do, it is found that at the age of 6 years the child should do a third of the work of an adult, and at 12, one-half. The average dose of work for an adult skilled worker is 44 hours a week. It is found that a child aged 12 does thirty hours of work at school, with from seven to fifteen hours of home work. Physicians thus allow a large overdose of work, nearly the full number of hours of work for adults. A striking evidence of this overwork is the great increase in self-destruction among high school and college students.

Preparation for complete living is the function which education has to discharge (Herbert Spencer). Any educational system from which the student enters life's work with the nervous system worn out does not fulfil its true function. The problem of adjustment will be difficult.

WILLIAMSON, New Orleans.

From the Analysis of a Bed Wetter. Anny Angel, Psychoanalyt. Quart. **4**:120, 1935.

Angel reports the analysis of a girl, aged 12 years, who suffered from enuresis following a severe and mysterious illness when she was about 3 years of age, which was characterized by violent spells of vomiting and possibly by fever. Before this she had been trained successfully in cleanliness. Analysis revealed that at that time, when her parents were away, she was staying with her grandmother and had made the acquaintance of a gipsy. The gipsy had lured her to his room and requested her to turn somersaults to expose herself. She had interpreted his laughter as ridicule of her genitals. He had then shown her his penis and had induced her to play with it and had played with her genitals. As a result of this she acquired the idea that her genitals were so defective that she could not control her urine, so that it must always flow out against her will. Urinary organs and genitalia were closely associated in her mind. She believed she urinated from the vagina and that a man had two penises, a flaccid one for urination and an erect one for intercourse. After analysis of this incident the enuresis ceased and remained absent for three years. The patient's mother interrupted treatment at this point, being satisfied with the clinical improvement, so that analysis was not completed. Pearson, Philadelphia. [Arch. Neurol. & Psychiat.]

The Child Guidance Clinic. Harvey Sutton, Brit. M. J. **2**:495 (Sept. 14) 1935.

The article includes a brief discussion of the problem child and the conditions which induce the problems, suggestions for the correction of the behavior and a brief statement of desirable locations for the holding of child guidance clinics.

Royster, University, Va.

The Psychoses of Adolescence. W. S. Dawson, Brit. M. J. **2**:651 (Oct. 12) 1935.

The various psychoses occurring at or near adolescence, with their treatment, are discussed. This article does not lend itself to abstracting.

Royster, University, Va.

The Strain of School Life on Girls During the Early Menstrual Period. D. J. Gair Johnston, Brit. M. J. **2**:892 (Nov. 9) 1935.

As the author states, this article is "a condensed account of an inquiry, carried out at the request of an educational authority, to determine the effect of the strain of school life on the physical welfare of girls during the somewhat critical period of the early menstrual years, with special reference to home lessons." The result of this inquiry is summed up in the following conclusions of the author: (1) Between the ages of 12 and 15 years the physical development of girls is much more rapid than that of boys; (2) sexual development in girls, with all its attendant disturbances, is very active during this period; (3) this rapid physical and sexual development of girls coincides with a strenuous educational effort; (4) the investigation shows that the standard of fitness of girls is lower than that of boys and that it depreciated more during the winter session when examinations were made; (5) home lessons require a greater expenditure of energy from girls, and (6) this is a period when the health of girls requires to be carefully guarded.

Royster, University, Va.

A Survey of Mongolism, with a Review of One Hundred Cases. Elizabeth N. Warner, Canad. M. A. J. **33**:495 (Nov.) 1935.

The author gives a comprehensive review of the literature on mongolism. The data given for the one hundred cases correspond well with the data cited from

the literature. Approximately half the children in this series died while under observation, the average age being 12.6 months. In 56 per cent of the cases the cause of death was bronchopneumonia. The next most common cause of death was congenital heart disease—in 7 per cent of the cases.

In 34 per cent of the children in this series there was some defect other than the deformities characteristic of mongolism. Thirteen per cent of the children had congenital heart lesions, 5 per cent had hernia (exclusive of umbilical hernia), and 3 per cent, clubfoot. In a control group of one hundred infants selected at random from the wards there were congenital heart disease in only 2 per cent and other congenital defects in 5 per cent. This article presents an excellent discussion of mongolism.

MOORE, Omaha.

EDUCATIONAL AND STATISTICAL DATA ON CHILDREN OF ABNORMAL MENTALITY IN THE ELEMENTARY SCHOOLS OF FLORENCE. V. UGUCCIONI, Riv. di clin. pediat. **33**:1245 (Nov.) 1935.

In a brief historical outline Uguccioni reports that the first institution in Italy for the education of abnormal children was established in Aosta in 1848; it accommodated the cretins in this region, and the asylum was closed after a short existence. In 1884 an asylum for the education of imbecile and idiot children was established in Sicily but was later transformed into a custodial institution. The first real educational institution for feebleminded children was established in Liguria, in 1889. Then other institutions were built in Milan, Alexandria and Rome.

INFANTILE PSYCHOLOGY. OSWALDO GUIMARES, Arch. de pediat., Rio de Janeiro **7**:665 (Aug.) 1935.

The author discusses some problems of infant psychology.

SANFORD, Chicago.

EDUCATION OF THE NURSING CHILD. ERNESTO CACACE, Med. de los niños **36**:265 (Sept.) 1935.

The author believes that education of the child should take place in the home and that, therefore, the mother must be taught to understand the child and his problems. For this purpose an institute of nepiology should be established. The morbidity and mortality rates cannot effectively be reduced without such an agency.

DWYER, Kansas City, Mo.

TRAINING DIFFICULTIES SEEN UNDER THREE THERAPEUTIC ASPECTS. MALWINE LÖWY, Ztschr. f. Kinderpsychiat. **2**:140 (Dec.) 1935; **2**:174 (Feb.) 1936.

This is a comprehensive discussion of the behavior of the asocial child with particular reference to incorrigibility in later years of childhood and early youth. Pedagogic psychology, psychoanalysis and the individual psychology of Adler are evaluated in their therapeutic effectiveness as applied to disorders of conduct. Typical cases are presented critically. The problem is a serious one in that it involves the social destructiveness of the subject and in turn affects society. Half-educated parents and self-styled psychoanalysts are at times responsible for incorrigibility in children under their guidance or influence.

The principles of psychotherapy advocated by Freud or by Alfred Adler are at times effective (generally greater success is observed in boys than in girls). Properly applied educational psychology has its place in the treatment of these disorders but only to the extent that it keeps the children occupied and away from evil. Basically and logically treatment of serious behavior disorders should be under the supervision of the physician trained in understanding the child—his physical, mental and emotional life.

JAHR, Omaha.

Diseases of the Genito-Urinary Tract

RENAL DWARFISM: A CASE REPORT. J. F. ROBERTS, Ann. Int. Med. **9**:1729 (June) 1936.

A case of renal dwarfism in a boy aged 8 years is reported. An unexplained dilatation of the urinary tract was present. In addition, the pituitary gland weighed only 0.2 Gm. It showed no evidence of a tumor. The anterior and posterior lobes were normal in proportion to each other.

On the basis of these findings it is postulated that the dwarfism in this case might have been of pituitary origin as a result of changes produced in the pituitary gland by some product of altered metabolism arising as a result of the long-standing renal insufficiency.

READING, Galveston, Texas.

INTRAVENOUS SUCROSE AS A DIURETIC. J. GUY STROHM and S. B. OSGOOD, Northwest Med. **35**:89 (March) 1936.

In 1923 Keith used hypertonic sucrose to produce dehydration in experimental animals. It has been used widely to reduce increased intracranial pressure. In several cases in which intravenous dextrose, caffeine and alkalis were inefficient, Strohm and Osgood gave 50 per cent sucrose in doses of from 20 to 50 cc. and produced marked diuresis.

SCOTT, Philadelphia.

SUCCESSFUL TREATMENT BY MEANS OF MANDELIC ACID OF A CHILD WITH URINARY STASIS AND INFECTION. H. F. HELMHOLZ, Proc. Staff Meet., Mayo Clin. **11**:231 (April 8) 1936.

A child who had pyelitis, megalo-ureters, hydronephrosis on the right and ureteral stenosis on the left and whose urinary tract contained innumerable Escherichia coli was freed from bacillary infection in the course of ten days by the administration of sodium mandelate, in doses of 1.25 Gm., and ammonium chloride, in doses of 0.5 Gm., given four times a day by mouth.

MILLER, South Bend, Ind.

RENAL DWARFISM. R. L. J. KENNEDY, Proc. Staff Meet., Mayo Clin. **11**:289 (May 6) 1936.

Seven cases are reported in which the patients showed the characteristic findings of retarded growth, retarded skeletal development and impaired renal function with resultant polyuria, polydipsia, albuminuria, azotemia, hyposthenuria and hyperphosphatemia. The striking skeletal changes are divided into three types: (1) the atrophic type, in which the bones are fragile, atrophic and osteoporotic, lines of cancellous tissue are present in the epiphysial ends of the diaphysis, and a thin, atrophic cortex and fractures of the shaft are present; (2) the florid type, in which the changes are characteristic of florid rickets, and (3) the woolly, stippled or honeycomb type, in which the epiphysial ends of the shaft are swollen. There is some osteoporosis, but the cortex is not thin as in the atrophic type. Metaphysial changes may not be uniform in all the bones.

MILLER, South Bend, Ind.

PYELONEPHRITIS IN CHILDREN DUE TO BACILLUS COLI INFECTION. AMERICO VALERIO, Arch. de méd. d. enf. **39**:225 (April) 1936.

The fundamental characteristics of this condition in the very young are the persistent high temperatures and the total absence of objective and subjective symptoms relating to the urinary apparatus, aside from the laboratory findings. A further point of interest is the divergence of views on treatment. French clinicians, following the method of Nobécourt, recommend measures which tend to increase the acidity of the urine in the belief that the growth of the colon bacillus is thus inhibited, while the English school advises alkalization of the urine

for the same purpose. In addition to these measures the usual management of infective processes is followed by both groups in the exhibition of baths, packs, stimulants, intravenous injections of dextrose, diuretics, etc.

Bayma strongly advises transfusion, while others report excellent results from serotherapy and the use of vaccines and dyes.

Valerio reports a case in an infant of 10 months to illustrate his results in a series of forty, in which he used a colon bacillus vaccine combined with injections of 10 units of insulin daily. Of these children, thirty-nine are reported as definitely cured after one month's treatment. AMESSE, Denver.

MEASLES IN GLOMERULONEPHRITIS WITH A NEPHROTIC SYNDROME. R. S. SANTIAGO and R. PEREIRAS VALDES, Arch. de med. inf. **5**:186 (June) 1936.

In a case of glomerulonephritis the condition was little influenced by the classic treatment. When measles developed there was an improvement in the clinical, renal and humoral syndromes. SANFORD, Chicago.

DEMONSTRATION OF TUMOR OF THE BLADDER BY MEANS OF CONTRAST PNEUMOGRAPHY. I. TAGER and M. SANTOCKIJ, Fortschr. a. d. Geb. d. Röntgenstrahlen **53**:882 (June) 1936.

The authors fill the urinary bladder with a specially prepared rather thick suspension of barium. After a short time the suspension of barium is removed and the bladder distended with air. In this manner satisfactory silhouettes of the inner surface of the bladder and of objects within the vesical cavity are obtained. It is possible that this technic might be applied with profit to the study of diverticula and of trabeculation of the bladder in children.

McCUNE, New York.

NEPHROLITHIASIS IN CHILDHOOD.. T. HALBERTSMA, Maandschr. v. kindergeneesk. **5**:89 (Dec.) 1935.

Two cases of this condition observed in boys are described and the present conceptions on the etiology of nephrolithiasis are discussed.

VAN CREVELD, Amsterdam, Netherlands.

Diseases of the Ductless Glands; Endocrinology

THE FILTERABLE CALCIUM OF BLOOD SERUM: I. A COMPARISON OF FILTERABLE CALCIUM OF SERUM AND TOTAL CALCIUM OF CEREBROSPINAL FLUID IN NORMAL HYPERPARATHYROID AND HYPOPARATHYROID STATES. RAYMOND GREGORY and MARIE ANDERSCH, Am. J. M. Sc. **191**:263 (Feb.) 1936.

Estimations of the total and filtrable calcium of the serum and of the total calcium of the spinal fluid were made in nine persons with normal calcium metabolism. A series of comparisons of the total and filtrable calcium of the serum with the total calcium of the spinal fluid was made in two cases of hyperparathyroidism and two cases of hypoparathyroidism. The filtrability of the calcium of the spinal fluid was also studied in subjects with normal and abnormal calcium metabolism. The filtrable calcium of the serum is elevated in hyperparathyroidism and lowered in hypoparathyroidism. The filtrable calcium of the serum and the total calcium of the spinal fluid are usually practically equal over the normal range of serum calcium values. In two of nine persons in the normal series, however, the filtrable calcium of the serum exceeded the total calcium of the spinal fluid by an amount greater than the usual experimental error. The calcium level in the spinal fluid was slightly elevated in one case of hyperparathyroidism and normal in another case. It was also normal in two cases of hypoparathyroidism. Wide variations in the values for the filtrable calcium of the serum may

occur without any change in those for the calcium of the spinal fluid. It is proper, therefore, to question all values for the filtrable calcium of the serum which are obtained by estimating the calcium of the spinal fluid. The calcium of the spinal fluid is completely filtrable. It was impossible to raise the total calcium of the serum above 7.6 mg. in one case of hypoparathyroidism by administering 4 cc. of parathyroid extract and 4 Gm. of calcium lactate daily, but the symptoms and signs of tetany were completely relieved. In one proved case of hyperparathyroidism the maximal change in the serum calcium values occurred within three days after the removal of a parathyroid adenoma. This should be kept in mind in using the value for the serum calcium as the criterion of success in the surgical treatment of parathyroid adenoma.

HENSKE, Omaha.

DISTURBANCES OF THE ENDOCRINE BALANCE AND THEIR RELATION TO DISEASES OF METABOLISM. C. N. H. LONG, Ann. Int. Med. **9**:1619 (June) 1936.

Following a short discussion of the interrelationship between the anterior lobe of the pituitary gland and the other organs of internal secretion, factors which modify experimental diabetes were considered in the light of their relationship to diabetes mellitus in man.

A better understanding of the diseases of metabolism associated with disturbed endocrine function could be reached by ceasing to regard them merely as alterations in function limited to one endocrine organ; they should be considered rather as disturbances of the equilibrium existing between all the organs of internal secretion.

READING, Galveston, Texas.

THE LAURENCE-MOON-BIEDL SYNDROME: REPORT OF THREE CASES. M. MOLITCH, R. G. GLADDEN and A. W. PIGOTT, Endocrinology **19**:682 (Nov.-Dec.) 1935.

Since this syndrome was described first in 1866 by Laurence and Moon and later by Biedl in 1922, almost a hundred cases have been reported in the world's literature. The syndrome consists of six cardinal symptoms: obesity, mental deficiency, genital dystrophy, polydactylism, retinitis pigmentosa and familial occurrence. None of the three boys whose condition is reported in this paper had all the six symptoms, yet all of them would qualify as subjects of the disease if obesity and genital dystrophy were grouped under the head of "pituitary dysfunction." Two of these boys had the Fröhlich type of dystrophy, while the third was short and obese, with the feminine distribution of hair and fat. Polydactylism is said to have been present in a paternal grand-uncle. Two boys had a high grade of myopia, while only one had retinitis pigmentosa. Polydactylism, mental deficiency, pituitary dysfunction and some visual defect were present in all three.

Since Reilly and Lisser in their review found that all the six cardinal symptoms were present in only twenty-five of seventy-seven cases, the authors believe that partial clinical combinations deserve recognition, provided that there is familial occurrence.

JACOBSEN, Buffalo.

THE RELATIONSHIP OF THE ANTERIOR PITUITARY GLAND TO THE THYROID AND OVARY. L. LOEB, J. SAXTON and S. J. HAYWARD, Endocrinology **20**:511 (July) 1936.

It has been shown that extracts of the anterior lobe of the pituitary gland produce widely different effects depending on what test animal is used. A new method is described for studying these effects: Individual anterior lobes of pituitary glands are immersed in various solutions such as water, 0.9 per cent sodium chloride, alcohol, ether, etc., and subsequently implanted in test animals. As a result of this preliminary treatment the anterior lobes undergo changes, which may be demonstrated by their effects on the thyroid glands and ovaries of the test animals.

Experiments are described which indicate that there exists, in addition to the hormone causing maturation and the hormone producing luteinization, a substance in the anterior lobe of the pituitary gland, mainly in that of the ox, the sheep and

the pig, which causes rapid destruction of follicles in the guinea-pig's ovary. This substance they have designated "atresin." Evidence is found that these three hormones act independently of each other, but atresin may hide the action of the others.

By the method described it is possible to transform the anterior lobe of the pituitary gland of one species so that in its effects it resembles that of another species.

JACOBSEN, Buffalo.

ASSAY OF BLOOD AND URINE FOR THYREOTROPIC HORMONE IN THYROTOXICOSIS AND MYXEDEMA. S. HERTZ and E. G. OASTLER, Endocrinology **20**:520 (July) 1936.

A new method of assaying the thyrotropic factor in blood and urine is described. Pituitarectomized rats are given injections of the test material for five days; on the tenth day the thyroid glands are examined histologically. Support of the thyroid gland against the histologic changes following pituitarectomy is considered evidence of a positive test, while failure of the injected material to prevent the retrogression of the thyroid epithelium is considered evidence of a negative test.

It was found by this method that blood serum and urine from myxedematous patients contain appreciable quantities of thyrotropic material, whereas none of the thyroid-stimulating factor could be demonstrated in the body fluids of either thyrotoxic or normal persons.

With the foregoing data in mind the authors find it difficult to accept the so-called anterior pituitary hypothesis in its present form as an explanation of the pathologic mechanism of human exophthalmic goiter.

The urine of patients with myxedema offers an excellent source of thyrotropic material for purposes of purification and chemical identification.

JACOBSEN, Buffalo.

PITUITARY INFANTILISM. SYDNEY JACOBS, New Orleans M. & S. J. **88**:506 (Feb.) 1936.

Jacobs reports the cases of two adolescent girls aged 15 and 16 years, respectively, each of whom had delayed menstruation, headaches and short stature.

Under therapy with anterior pituitary extract given hypodermically, menstrual regularity was established, and some growth occurred. The growth reported was less than average for normal children of corresponding ages. Menstruation is often delayed to these ages and becomes normal without treatment. No record is given for the rates of growth prior to treatment.

While improvement occurred during the therapy, no proof is shown that the hormone was the responsible factor. Similar improvement can occur and has occurred spontaneously.

BERKLEY, Los Angeles.

THE TREATMENT OF A TYPE OF MALNUTRITION (SIMMONDS' DISEASE LIKE) WITH PREPITUITARY GROWTH HORMONE. LOUIS BERMAN, New York State J. Med. **35**:916 (Sept. 15) 1935.

Twenty-four patients with a condition suggestive of pituitary insufficiency were treated with standardized extract of the anterior lobe of the pituitary gland containing the growth hormone. The ages of the patients are not given, but the weights show that most of the patients were adults. There was an average gain of about 32 pounds (14.5 Kg.) in from three to six months.

AIKMAN, Rochester, N. Y.

RELATIONSHIP OF THE PITUITARY GLAND TO CARBOHYDRATE METABOLISM. A. B. CORKILL, M. J. Australia **1**:168 (Feb. 1) 1936.

The history and development of knowledge of the anatomy and physiology of the pituitary gland are reviewed by Corkill. The striking action of posterior

pituitary as an inhibitor of the hypoglycemic action of insulin is utilized by him in combating hypoglycemia. He cites the experiments of Lawrence, whose work indicates that the dextrose-mobilizing effect of posterior pituitary is exerted on the liver glycogen, but only in conditions of emergency. It has no effect in the normal subject. Repeating the experiments which Houssaye performed on hypophysectomized dogs, Corkill and his co-workers were able to confirm Houssaye's findings in the rabbit. They showed that removal of the pituitary gland rendered the animals hypersensitive to the hypoglycemic action of insulin. It was found to be extremely difficult to bring about recovery from the hypoglycemic state with dextrose, epinephrine and posterior pituitary. Houssaye's work demonstrating that glycosuria following pancreatectomy was much less in hypophysectomized animals than in normal controls or in animals with only the posterior lobe removed is also cited. Further study of these hypophysectomized animals revealed a normal amount of epinephrine and as high as 6 per cent of hepatic glycogen. From these findings it was concluded that although glycogen was present it was resistant to mobilization by epinephrine. Apparently hypophysectomy interferes with the normal mechanism concerned with the protection of the body from hypoglycemia. In the absence of anterior pituitary epinephrine is unable adequately to transform glycogen to dextrose, and the power of the pituitary to accelerate the formation of dextrose from protein is depressed.

Corkill concludes by questioning the relationship between pituitary dysfunction and obesity but feels that most experimental evidence points to an anterior lobe hormone that is actively concerned with fat metabolism.

GONCE, Madison, Wis.

STUDY AND DIAGNOSIS OF ENDOCRINE DYSFUNCTION IN SCHOOL CHILDREN. L. MORINSON, J. de méd. de Paris **56**:14 (Jan. 9) 1936.

This brief review of endocrine disturbances observed in school children is valuable in suggesting to the teacher and the school physician indications of abnormal endocrine function in the physical condition and mental activity.

LESLIE, Evanston, Ill.

DIABETES INSIPIDUS IN EARLY CHILDHOOD. CARLOS GIANELLI, Arch. de pediat. d. Uruguay **7**:61 (Feb.) 1936.

Gianelli reports a case of diabetes insipidus in an infant aged 16 months. Marked polydypsia and polyuria were striking symptoms. The urine showed both albumin and sugar. A roentgenogram of the skull was normal. There were no ocular symptoms. Injection of extract of the posterior lobe of the hypophysis caused marked amelioration of the symptoms for a brief period. The child died of acute bronchopneumonia eight days after admission to the hospital.

SCHLUTZ, Chicago.

DYSTROPHY ADIPOSOGENITALIS. L. VIAMONTE CUERVO, Bol. Soc. cubana de pediat. **8**:105 (March) 1936.

The author presents eight cases of the adiposogenital syndrome. All the patients showed the peculiar feminine distribution of the fat. Ectopy of the testicles was generally present. There were certain mental abnormalities, expressed mainly in lack of concentration, weakness of will power, timidity and lack of initiative.

In all the patients there was definite hypotonicity of the muscles with flaccidity of the tendons. All had flat feet. Adrenal function seemed to be deficient. All definitely gave the impression of hypophyseal insufficiency. In four there was a definitely low basal metabolic rate.

The author discusses the possibility of a thyrotropic insufficiency of the prehypophysis. One of the patients seemed to present some evidence of a possible neoplasm of the hypophysis. Syphilis was present in the antecedents of two of the subjects.

SCHLUTZ, Chicago.

THE THYMUS AND SUDDEN DEATH IN INFANTS. MARTÍNEZ VARGAS, Med. de los niños **37**:65 (March) 1936.

The author begins with a reference to the cases of sudden death caused by the thymus and with the statement that newly born infants should have roentgen treatment for an enlarged thymus. The thymus gland is described, and the various theories regarding the mechanism by which this organ produces symptoms are mentioned. The author is inclined to the view that death is the result of asphyxia from pressure on the trachea in the majority of the cases.

DWYER, Kansas City, Mo.

THE PINEAL SYNDROME. JOSÉ BOIX BARRIOS, Pediatría españ. **25**:71 (March) 1936.

The author reports a case of the pineal syndrome, which is comparatively rare, in a girl aged 9 years. Always retarded both mentally and physically, she began to show mass growth and overdevelopment at the fifth year and had full sexual development with irregular menstruation from the eighth year. Except for chronic cephalalgia no demonstrable symptom pointed to involvement of the pineal gland, although this was suspected to be the chief etiologic factor.

The author expresses the opinion that macrogenitosomia and hypergenitalism do not necessarily indicate disease of the pineal gland if such a disorder cannot clearly be demonstrated. Symptoms which would definitely indicate pineal disorder are hypergenitalism, hydrocephalus, obesity and visual symptoms.

SCHLUTZ, Chicago.

LATENT TOXICOSIS AND DIABETES INSIPIDUS. ANNA VON SZÁSZ, Monatschr. f. Kinderh. **65**:296 (April) 1936.

Von Szász reports two cases of alimentary intoxication in which the condition was cured by recognition and treatment of underlying diabetes insipidus. The author repeats that one should not overlook endocrine disturbances in conditions which one diagnoses clinically as nutritional disease. GERSTLEY, Chicago.

LIPODYSTROPHIA TRAUMATICA. G. H. MONRAD-KROHN and RAGNAR FORSBERG, Norsk mag. f. lægevidensk. **97**:249, 1936.

Lipodystrophia progressiva (Simon's disease) is a clinical entity which was described by Simon in 1911 in an article entitled "Eine seltene Trophoneurose."

Simon's patient was a 21 year old woman who during a period of ten years had shown slowly progressive loss of fat from the face, upper extremities and trunk. During the later five years a considerable layer of fat was observed on the buttocks and upper parts of the thighs. Simon thought that this disease was a result of a disturbance in the internal secretion with special reference to the fat tissue.

In the present article the authors describe a 38 year old woman in whom lipodystrophia developed after two traumas to the head. After traumatic meningopathy, headache and dizziness, the layer of fat disappeared from the face, chest and upper extremities. They consider the pathologic condition a result of a traumatic lesion of the hypophysis or of the parahypophysial tissue.

TOVERUD, Oslo, Norway.

Diseases of the Muscles, Bones, Joints and Lymph Glands

CONGENITAL BONY TEMPOROMANDIBULAR ANKYLOSIS AND FACIAL HEMIATROPHY. L. W. BURKET, J. A. M. A. **106**:1719 (May 16) 1936.

Bony ankylosis of the temporomandibular joint associated with mandibular hemiatrophy is sufficiently rare to warrant a report. Burket describes a case in

which the fibrous and bony fixations were freed twenty-four hours after birth. A recurrence was noted in two months, but a sufficient opening remained to permit adequate feeding. No other report of this was found recorded.

BONAR, Salt Lake City.

TRANSITORY SYNOVITIS OF THE HIP JOINT IN CHILDHOOD. J. G. FINDER, J. A. M. A. **107**:3 (July 4) 1936.

Although of relatively frequent occurrence, transitory synovitis of the hip joint in childhood often escapes diagnosis. It is often mistakenly diagnosed as tuberculosis of the hip. Finder discusses twenty-two cases observed since 1916, seven in the past two years. The disease occurs usually in children under 8 years. They have pain, muscle spasm and a limp. There is moderate elevation of the temperature and of the white blood cell count. Roentgen examination usually reveals nothing. The treatment should be conservative, consisting of rest, traction or immobilization and later physical therapy. The prognosis for functional recovery is good.

BONAR, Salt Lake City.

ANTISTREPTOLYSIN TITERS IN RHEUMATOID ARTHRITIS. M. H. DAWSON and M. OLMSTEAD, Proc. Soc. Exper. Biol. & Med. **34**:82 (Feb.) 1936.

The antistreptolysin titer was found to be increased in the forty cases of rheumatoid arthritis which were of less than one year's duration and especially in those in which there had been an acute or subacute onset, whereas in one hundred and fifty-one late cases (of more than one year's duration) essentially normal values were found.

HANSEN, Minneapolis.

RHEUMATOID ARTHRITIS. G. L. KERR PRINGLE, Brit. J. Phys. Med. **10**:173 (Feb.) 1936.

Pringle discusses various physical methods for the treatment of rheumatoid arthritis. Heat, massage, ultraviolet rays, diathermy, baths and spa treatments are considered.

HARTMAN, Cleveland.

JUVENILE OSTEOCHONDRITIS DEFORMANS. RAFAEL PEÑALVER, Cir. ortop. y traumatol. **2**:195 (Oct.) 1934.

Peñalver reports eleven cases of juvenile osteochondritis of the hip. He concludes that Legg-Perthes' disease is a static infection, and, as in all other ailments of this type, the bone is deficient from birth, while deformity ensues as soon as the deficient part of the skeleton is called on to bear the body weight. He found no causal relation between this disease and rickets, syphilis, tuberculosis or other disorders, though they might accompany it. It is far more frequent in the male between the ages of 4 to 10 years than in the female and is seldom found bilaterally. Common signs include limited abduction and inner rotation of the hip; roentgenograms show valuable signs. The prognosis is favorable, but the limb might be shortened, which can be remedied by orthopedic treatment. Treatment includes immobilization for from three to four months in a cast and plaster spica and lifting the sound foot 1½ inches (3.8 cm.) from the ground. The patient is kept under close scrutiny after the cast is removed, and if any signs of impairment appear immobilization is carried out again. Calcium is given, with cod liver oil and ultraviolet irradiation.

HERRON, Spokane, Wash.

HEMOPTYSIS CAUSED BY OSTEITIS OF A RIB. A. AMORIM, J. de pediat., Rio de Janeiro **3**:178 (April) 1936.

In a child of 7 years there were no symptoms except severe hemoptysis. Roentgenograms showed involvement of the seventh rib, and it was found that the process had eaten into a pleural vessel. The condition was presumed to be syphilitic.

SANFORD, Chicago.

RETICULOCYTES IN LYMPHATISM. CHARLOTTE HÜLSZE, Arch. f. Kinderh. **105**:73, 1935.

In a study of twenty-nine cases of lymphatism in children a relative increase in monocytes and lymphocytes was evident, while the total white cell count was unchanged from the normal. An increase in the reticulocytes was observed only in those cases in which mild anemia was present. It appears questionable, therefore, whether an increase in reticulocytes can be accepted as a criterion of lymphatism.

CRANE, Chicago.

CALCIFIED MESENTERIC GLANDS. HARALD BOCK, Monatschr. f. Kinderh. **65**:73 (March) 1936.

Bock presents case histories and roentgenograms to show that calcified mesenteric lymph nodes can be demonstrated by the roentgen rays. A roentgenogram taken in the ventrodorsal position is satisfactory. The source of the tuberculosis is probably a primary lesion in the intestine, although the patients frequently showed involvement of the cervical lymph nodes. In all these cases the source of the tuberculosis was probably the gastro-intestinal tract.

GERSTLEY, Chicago.

VITAMIN C AND PROGRESSIVE MUSCULAR DYSTROPHY. Y. HIRATA and K. SUZUKI, Orient. J. Dis. Infants **18**:355 (Nov.) 1935.

Noting the similarities of pathologic as well as chemical changes in the tissues between progressive muscular dystrophy and certain types of virulent intoxication such as that due to diphtheria toxin or tetanus toxin, the authors studied the effect of the parenteral administration of vitamin C in various types of conditions in which there was atony of the musculature. The following observations are recorded: 1. The excretion of creatinine and creatine began to decrease within a week after the administration of vitamin C, and the creatine-creatinine ratio was restored to the normal value. 2. The high value for blood phosphorus, due to an increase in the inorganic phosphorus content as seen in patients with muscular atrophy, returned to the normal level after the administration of vitamin C. 3. A peculiar sensation of itching and spastic contraction of the affected muscles developed regularly in these patients at a definite time after the beginning of the vitamin C therapy. 4. A decrease in the value for chronaxia in the muscles of the leg (the gastrocnemius muscle and the anterior tibialis muscle) occurred until a normal level was reached. 5. The administration of vitamin C, furthermore, brought about an increased ability of various muscles to function more or less normally, and tendon reflexes also showed marked improvement. A further study is in progress.

KATO, Chicago.

Diseases of the Eye

RESULTS OF CERVICAL SYMPATHECTOMY IN PIGMENTARY DEGENERATION OF THE RETINA. FRANK B. WALSH and LOUISE L. SLOAN, Arch. Ophth. **14**:699 (Nov.) 1935.

Three patients with pigmentary degeneration of the retina were subjected to operation on the cervical sympathetic trunk, without benefit in two cases and with questionable benefit in the third. In two cases there were no improvement in vision, the fields or the light sense and no visible changes in the caliber of the retinal arteries. In the third case there were many complications from the sympathectomy, but the patient insisted that there was improvement in her visual fields and night blindness, although this could not be demonstrated.

WESCOTT, Chicago.

RELATION OF STRABISMUS TO RIGHT OR LEFT SIDEDNESS. W. H. FINK and BRYNG BRYNGELSON, Arch. Ophth. **14**:947 (Dec.) 1935.

The authors believe that strabismus is a dysfunction of the fusion centers related to dysfunction of other brain centers. They had called to their attention a 5 year old boy, who, while being treated for strabismus, began to stutter. He was left-handed, and the right eye was convergent. The child was instructed to use his right hand in drawing. After several weeks he began to stutter. The stuttering ceased as soon as the drawing with the right hand was stopped. In a series of sixty persons with convergent strabismus, 42 per cent were ambidextrous; 58 per cent were right-handed, and none was left-handed. Shift of handedness occurred in 60 per cent of the group, and there were speech defects in 40 per cent.

WESCOTT, Chicago.

THE CONSERVATION OF VISION IN THE CHILD. G. E. DE SCHWEINITZ, Pennsylvania M. J. **39**:774 (July) 1936.

Successful conservation of vision in children's eyes depends on the cooperation of the general physician, the pediatrician and the ophthalmologist and on the cooperation of the obstetrician. If it were possible to examine critically a hundred thousand blind people, it would be found that about a fourth of them had lost their sight by some infection or disorder that might have been checked. De Schweinitz reviews (1) corneal defects and their origin, (2) phlyctenular keratoconjunctivitis, (3) lacrimal obstruction (dacryocystitis), (4) refractive errors, (5) sight-saving classes and (6) strabismus.

It is the duty of the general practitioner and the pediatrician, when one or the other observes abnormalities which pertain to the eyes and their nerve connections, to refer the patient for expert examination, just as it is the duty of the ophthalmologist to call in the physician if the condition calls for physical examination.

LOGUE, Williamsport, Pa.

DWARFISM WITH RETINAL ATROPHY AND DEAFNESS. E. A. COCKAYNE, Arch. Dis. Childhood **11**:1 (Feb.) 1936.

Two cases are reported in which dwarfism was associated with deafness, retinitis pigmentosa and mental retardation. One patient was a girl of 7 years; the other was a boy of 6 years.

The two children were not related.

KELLY, Milwaukee.

POSTERIOR LENTICONUS AND FALSE LENTICONUS. ANTONIO ALCALÁ LÓPEZ, Arch. de oftal. hispano-am. **35**:505 (Oct.) 1935.

This is a report of a case of bilateral eccentric pseudolenticonus in which the optical and the clinical picture corresponded exactly to those described in previous reports of cases of posterior lenticonus, but in which an examination with the slit lamp showed a normal capsule and a normal position of the lenticular nucleus. After reference to the cases of Vogt, Riedl, Krasso and Jakobowicz, whose observations were confirmed by this method, and to the studies of Pergens, Bach, Beck, Hess and von Hippel, which show the nonexistence of lenticonus in eyes of rabbits and pigs clinically presenting the classic complex of symptoms, Alcalá López agrees with Dor in considering most of the reported cases of lenticonus as examples of pseudolenticonus.

He attributes the picture to a localized thickening of the lens with increase of its refractive index, possibly due to aberrant lenticular cells of an abnormal type, separated from the anterior epithelium during fetal life, which were preserved and which developed in the midst of the normal ones from the posterior epithelium, or to pathologic changes similar to the formation of refringent globules in flat cell epithelioma (cholesteatoma of Müller).

FINLAY, Havana, Cuba. [ARCH. OPHTH.]

GENEALOGIES IN TWENTY-EIGHT CASES OF HEREDITARY PIGMENTARY DEGENERATION OF THE RETINA. W. SCHEURLEN, Klin. Monatsbl. f. Augenh. **94**:761 (June) 1935.

Scheurlen has compiled the records in 506 cases of retinitis pigmentosa observed at the University Eye Clinic of Tübingen since 1877. Tables stating the names of the birthplaces of the patients show an even distribution over the neighboring counties. This indicates that the entire population is uniformly afflicted with the pathologic gene.

Consanguinity does not play the decisive rôle it has been credited with; it occurred in healthy branches of the families as well as in those in which some members suffered from retinitis pigmentosa. In some villages where the genealogies could be followed back to the middle of the seventeenth century, almost every one was ultimately related with the others. The affliction with the gene seems to have occurred in the whole population many centuries ago. The possibility exists that retinitis pigmentosa is a recessive hereditary process; positive proof cannot be established before the identity of the heterozygotes has been objectively established. The percentage of those afflicted remained unchanged during these fifty years. The genealogies show that 72 of the 94 diseased persons had no descendants. Only 22 had children and grandchildren, all of whom were healthy except that in genealogy 16 one woman had 2 diseased sons. "Sterilization of 92 diseased persons would have prevented up to date the birth of only 2 hereditarily diseased persons and of 237 phenotypically healthy persons." The fact that so many diseased persons had no descendants allows one to conclude that the relation between healthy and diseased genes changes slowly in favor of the healthy descendants.

STOLL, Cincinnati [ARCH. PATH.]

ANGIOMA OF THE CHOROID WITH NAEVUS FLAMMEUS OF THE TEMPLE: REPORT OF A CASE. A. LUDWIG, Klin. Monatsbl. f. Augenh. **95**:168 (Aug.) 1935.

In 1931, Lindenmeyer compiled a list of six cases of angioma of the choroid. In five of these cases the eyes were enucleated as presenting sarcoma of the choroid. In three other cases the symptoms pointed strongly toward the same disease, but histologic examinations could not be made as yet. In the remaining thirty-eight cases reported to date choroidal angioma was observed incidentally on histologic examination; the eyes had been enucleated for absolute glaucoma.

Ludwig's patient, a woman aged 28, was born with a hemangioma of the temple the size of a pea. In the course of time it grew to the size of a child's hand. The patient had no discomfort until headache set in two years prior to examination. Soon afterward the nevus assumed a darker hue, and vision failed in the left eye; temporal from the disk was a depigmented area of the retina, about 1.5 disk diameters in width. It showed a pigmented margin resembling the demarcation which occurs after a reattachment of the retina. In this case the retina was slightly detached, and the macular area was normal. Small yellowish white and strongly refracting "foam bubbles" were observed in the retina. In Ludwig's opinion, they may have been akin to the vacuoles in the inner granulated layer described by Reiss. The grayish blue color of the detached portion of the retina prompted him to interpret the lesion as an angioma. He considers this diagnosis corroborated by the presence of the facial nevus, the youthful age of the patient and the typical aspect of the demarcated area. According to Ludwig, the absence of degeneration of the macula and of a sector-shaped deficiency in the visual field, described by other authors, is to be explained by the peripheral location of the hemangioma.

STOLL, Cincinnati. [ARCH. OPHTH.]

GONOCOCCAL OPHTHALMIA. C. J. WU, C. H. TENG and C. C. WEN, Chinese M. J. **50**:59 (Jan.) 1936.

The writers report an epidemiological study coming from the department of public health, Peiping Union Medical College. In an institutional home for the poor in the city of Peiping, where the living quarters were crowded and dirty,

the inmates coming from the lowest strata of society, those in the age groups of 10 to 19 years and 50 to 59 years suffered the greatest percentage of infection. All the patients became infected after admission to this institution. The presence of a single case of gonorrhea with an active discharge, in addition to unhygienic conditions favorable for transmission, was considered sufficient to cause the epidemic of gonococcic ophthalmia. A common water-tank, a scanty quantity of warm water and the use of common towels would explain the spread of the ophthalmia. Twenty-one of the sixty patients lost one or both eyes.

The authors emphasize the importance of adequate hygienic conditions and medical care in public institutions.

NEFF, Kansas City, Mo.

THE POSTURE OF THE BULBUS OCULI IN PREMATURE INFANTS. T. SALMI and A. EEROLA, Acta pædiat. **18**:419, 1936.

The characteristically downcast and prominent appearance of the eyeball in the premature infant has received relatively little attention in either the literature or the textbooks of pediatrics; few explanations have been offered. Salmi and Eerola measured the diameter of the cornea, the width of the palpebral fissure and the diameter of the pupil, also the circumference of the head and of the chest in thirty-one premature infants. On a number of the infants the measurements were made serially from the neonatal period past the end of the second year. In this manner it was possible to establish a correlation between the position of the eyeball and the ratio of the circumference of the head to that of the chest: In general, exophthalmos and downcast eyes were found in every infant whose head had a circumference more than from 2 to 3 cm. greater than that of the chest. As the two measurements became more nearly equal the position of the eyes approached or reached the normal appearance found in full term infants. In many of the infants the peculiarity was found to be present during the first few weeks of life; in all it had disappeared by the end of the second year.

Anatomic studies revealed no difference in the conformation of the orbits between the premature and the full term infants. Further investigations of this matter are in progress. Despite the lack of anatomic explanation, the correlation described suggests that the peculiar posture of the eyes of premature infants is due to a relative disproportion between the growth of the brain, as reflected by the increasing diameter of the skull, and the growth of the skeletal system, represented by the diameter of the chest.

MCCUNE, New York

Skin Diseases; Allergy

TUMOR OF THE SKIN OF UNKNOWN ORIGIN: REPORT OF A CASE. FREDERICK REHM SCHMIDT, Arch. Dermat. & Syph. **32**:626 (Oct.) 1935.

Schmidt reports the case of a girl of 15 years with a rapidly growing button-like tumor on the dorsum of the left forearm. It was unaffected by roentgen radiation. Microscopic examination showed the epidermis to be intact and pushed out by a round mass of dark-staining cells clearly distinguished from the surrounding tissue. Under high magnification the nuclei were seen to be rodlike. The cells were fusiform, and their cytoplasm was denser than that of the surrounding fibroblasts. Mitoses were absent, and there was a moderate degree of nuclear anaplasia. The pathologic diagnosis was malignant leiomyoma, which Boyd stated seldom gives rise to metastases.

DULIN, Iowa City.

SIMPLIFIED METHOD FOR MEASURING THE SCALP PREVIOUS TO ROENTGEN EPILATION. RUBEN NOMLAND, Arch. Dermat. & Syph. **32**:631 (Oct.) 1935.

A simple method for measuring the scalp previous to roentgen epilation is described. This requires only a skin (eyebrow) pencil and a flexible celluloid ruler cut to a length of 5 inches (12.7 cm.). The time required to make the measurements is about thirty seconds.

DULIN, Iowa City.

SINGLE PUNCTURE METHOD OF TESTING WITH ALLERGENS. RAYMOND V. QUINLAN, Arch. Dermat. & Syph. **32**:631 (Oct.) 1935.

Quinlan used the scratch method in giving skin tests for allergens, then the multiple puncture method, as used in vaccination against variola. Now he advocates a single puncture. The allergen is applied as usual; then the needle is placed at 45 degrees, and a single puncture is made, the needle being elevated two or three times to allow the fluid to run between the layers of the skin. This method has been very satisfactory and does not leave the stains on the skin as scratching does, especially if done a little too deeply.

DULIN, Iowa City.

PSORIASIS WITH BULLAE: REPORT OF A CASE. OSCAR L. LEVIN and JESSE A. TOLMACH, Arch. Dermat. & Syph. **32**:718 (Nov.) 1935.

Levin and Tolmach report a case of a boy, 10 years old, who had circinate lesions on the anterior aspect of the thighs with the first outbreak of the eruption. These looked like ringworm, and when treated with iodine by the mother they promptly disappeared. Fifteen months later he had a similar but generalized rash along with some lesions showing definite vesicular and bullous elements in the center of the lesions. On the elbows were groups of papulosquamous lesions, which were typical of psoriasis. Photographs of the lesions of the hands and feet are included. Pathologic sections of the various lesions led the pathologist to believe that they were all of the psoriatic type. The case is reported because of the rareness with which bullous lesions occur in psoriasis.

DULIN, Iowa City.

FAVUS IN A NATIVE SCHOOL CHILD. PHYLLIS SCHUYLER, New York State J. Med. **35**:781 (Aug. 1) 1935.

A boy of 12 years had been under treatment for ringworm for two years. Microscopic and cultural examination proved the condition to be favus. "A plea is here made for the microscopic and cultural examination of all scaling diseases of the scalp in school children."

AIKMAN, Rochester, N. Y.

URINARY PROTEOSE IN DERMATOLOGY. S. E. LIGHT, Northwest Med. **34**:203 (June) 1935.

Light reports the clinical use of proteose obtained from the urine of allergic patients, prepared by the method of Oriel (*Lancet* **2**:406 [Aug. 1] 1933). Twelve patients were reported on, one aged 11 months and one, 12 years. A large number of injections was necessary. Local reactions of moderate intensity and an occasional general reaction with chills were observed. No improvement was seen in cases of urticaria. The best results were obtained with eczematous forms of dermatitis. There was often improvement or cure of the condition in spite of the continuation of offending foods.

SCOTT, Philadelphia.

FURTHER OBSERVATIONS ON PINK DISEASE. J. V. BRAITHWAITE, Arch. Dis. Childhood **11**:49 (April) 1936.

The further observations are that pink disease is caused by sensitivity to physical agents, especially heat and sunlight. Cooling the patients by light clothing, hydrotherapy and keeping them out of direct sunlight greatly reduces the mortality and shortens the course of the disease.

KELLY, Milwaukee.

SUPERFICIAL X-RAY THERAPY. ERNEST DORE, Brit. J. Phys. Med. **10**:74 (Sept.) 1935.

Dore discusses the results of his experience in the treatment of most of the common cutaneous disorders. The article is conservative.

HARTMAN, Cleveland.

THE TREATMENT OF PINK DISEASE. G. B. SWEET, M. J. Australia **1**:430 (March 28) 1936.

As the result of treating thirty-six consecutive patients with erythredema Sweet is of the opinion that all patients with the disease, whether mild or severe, provided that they are not admitted to a hospital, can be cured in a few weeks by ultraviolet radiation. Exposures to the radiation from the mercury vapor arc are given twice weekly, beginning with two minutes of exposure with the lamp 100 cm. from the patient and increasing the exposure to a maximum of ten minutes with the lamp placed 60 cm. distant. The patient is warmed by radiant heat (as from an electric heater) before, during and after the treatment with the radiation from the mercury vapor arc. Also the patient is turned from the recumbent to the prone position and back again at least every minute. Contrary to Braithwaite's experience of having only four of twenty-seven cases occur in the winter months, Sweet found the onset of the disease in twenty-eight cases to be evenly distributed through the year—summer, 8; autumn, 6; winter, 6; spring, 8.

GONCE, Madison, Wis.

A STUDY OF THE PERMANENT BACTERIAL FLORA OF CHILDREN'S SCALPS. MICHELINE DE BIEHLER, Arch. de méd. d. enf. **39**:157 (March) 1936.

Numerous investigations have indicated the existence of bactericidal substances in the skin and its adnexa. Reviewing his experiences with both human and animal subjects, Braun arrived at the following conclusions: 1. The skin and scalp of human beings and the hair of laboratory animals as well as human cerumen, contain definite protective bodies. 2. These bactericidal substances may be dissolved in alcohol, ether and acetone; if the method of Janek and Jörgensons is used, aqueous extracts from the human skin may also be obtained. 3. The extracts from hair and cerumen attenuate or wholly arrest bacterial growth on agar.

The term applied to these specific properties, as used by Hoffmann, is embraced in the general caption "esophylaxis." Biehler conducted a bacteriologic investigation of the hair of 100 children ranging in age from 1 to 14 years in one of the larger cities of Poland.

Of the samples placed in culture mediums only 9 per cent gave no growth; of those yielding a growth, 62 per cent showed invasions by Staphylococcus albus. The conclusion is reached that the presence of so-called protective substances in these areas has not been clearly demonstrated.

AMESSE, Denver.

DISSEMINATED GANGRENE OF THE SKIN IN EARLY CHILDHOOD. R. TURQUETY, J. de méd. de Paris **56**:9 (Jan. 9) 1936.

Primary gangrene of the skin occurring in debilitated infants is described. The anatomicopathologic and bacteriologic changes and the theories of pathogenesis are discussed. In the cases reported by the author no organisms were observed in the lesions, although the pneumococcus was isolated from the blood. The author, however, thinks that the pneumococcus was not the cause of the gangrene but that it was present in association with terminal pneumonia.

LESLIE, Evanston, Ill.

GENERALIZED INTERSTITIAL CALCINOSIS IN A CHILD AGED FIVE YEARS. PIAGGIO GARZON and J. A. SOTO, Arch. de pediat. d. Uruguay **7**:66 (Feb.) 1936.

A child 5 years of age with generalized interstitial calcinosis received excessively large doses of a solution of two calcium salts, chloride and lactate, for several years. Nodular masses appeared over the sacrococcygeal region and the gluteal muscles. Similar masses were also noted in the muscles of the leg and the muscles of the forearm, especially in the bend of the elbows, at the humeral insertion of the pectoral muscles and in the various muscles of the neck. The masses varied in size and were superficial, freely movable and painless.

Biopsy showed the masses to consist largely of fat infiltrated with deposits of calcium and surrounded by fibrous tissue. The generalized infiltration, especially about the extremities, caused marked limitation of motion.

The blood calcium content was 12 mg. per hundred cubic centimeters, and the phosphorus content was 4.3 mg.

The authors doubt whether the prolonged use of the calcium salts played any particular rôle in the production of the pathologic process.

SCHLUTZ, Chicago.

TREATMENT OF VON RECKLINGHAUSEN'S DISEASE WITH PLURIGLANDULAR PREPARATIONS. S. OGAWA, J. Pediat. (Tokyo), no. 430, Feb. 20, 1936, p. 420.

Ogawa reports a case of neurofibromatosis in a boy 10 years and 9 months of age, in which remarkable improvement in the clinical manifestations followed a year's treatment with pluriglandular preparations. KATO, Chicago.

CLINICAL AND STATISTICAL STUDIES OF IMPETIGO ALBOSTAPHYLOGENES (DOHI). H. ASANO, Jap. J. Dermat. & Urol. **38**:271 (Aug.) 1935.

Asano made a study of 165 cases of impetigo "albostaphylogenes (Dohi)"; she found that the condition is rare before the fourth month of postnatal life and that after the second year it is less frequent, becoming extremely rare after the sixth year.

Histologic examination of the lesion discloses the line of separation of the vesicle to be in the granular or in the malpighian layer, though the epithelial pegs were never either edematous or elongated. The content of the vesicle consisted of fibrin, moderate numbers of polymorphonuclear leukocytes and, rarely, mononuclears and swollen epithelial cells. A moderate amount of dilatation of the vessels and a mild perivascular infiltration were present, the cellular constituents corresponding to those of the aforementioned vesicular content. Bacteriologically, the staphylococci were present mostly within the leukocytes or in the vesicular fluid. During the course of one case the coincidental appearance of an eruption of measles produced a condition resembling ecthyma gangraenosum. Photographs of microscopic sections and of lesions accompany the article.

J. W. BRENNAN, Chicago. [ARCH. DERMAT. & SYPH.]

A SUPPLEMENTARY VIEW TO THE THEORIES ON ANAPHYLACTIC SHOCK. Y. SHINOMIYA, Orient. J. Dis. Infants **18**:33 (July) 1935.

Shinomiya observed that following a shock-producing operation in young rabbits there was a marked increase in the hydrogen ion concentration of the body fluids, a rise in the body temperature and some changes in the blood sugar level. These changes were minimized by an injection of a vitamin B preparation or of a sodium salt of bile acids. KATO, Chicago.

A CASE OF ERYTHROMELALGIA IN A CHILD. A. MIWA and C. NISHIMURA, Orient. J. Dis. Infants **18**:341 (Nov.) 1935.

The case of a boy 7 years and 9 months of age with erythromelalgia who made a complete recovery following eight injections of epinephrine hydrochloride (from 0.1 to 0.2 cc. of a 0.1 per cent solution) is reported. The patient showed a typical symptom complex consisting of paroxysmal pain, erythema, edema and local heat in the extremities, and examination of the capillaries by means of a capillary microscope revealed dilated and tortuous vessels during the height of the disease, the condition of the vessels returning to normal with the disappearance of the symptoms. The authors regard the disease as due to a disturbance of the vegetative nervous system. KATO, Chicago.

POSTPRIMARY ERYTHEMA NODOSUM. ARVID WALLGREN, Acta tuberc. Scandinav. **9**:1, 1935.

A positive reaction to tuberculin associated with erythema nodosum appears as a rule at the same time as the first tuberculous manifestation in the organism at the termination of the period of incubation (primary erythema nodosum tuberculosum). Sometimes it appears in persons who have reacted positively to tuberculin for a long time; the erythema then may be due to a secondary rise of the allergic response (postprimary erythema nodosum tuberculosum), or it may be caused by an agent which has nothing to do with the existing tuberculous infection (nontuberculous erythema nodosum). Wallgren reports fourteen cases of postprimary erythema nodosum tuberculosum. In four the erythema developed from one to two days after measles, in five cases from three to four weeks after the beginning of whooping cough, in four cases after tonsillitis and in one case during an attack of enterocolitis. There was an aggravation of the preexisting tuberculous lesion in only two cases (after measles); in the twelve remaining cases the tuberculous state was unchanged. The course of the postprimary type, as a rule, is much shorter than that of the primary type. Taking everything into consideration, there is therefore reason to regard the prognostic outlook in the postprimary type of the disease as much brighter than that in the primary type, as far as the length of the necessary care and the probabilities of simultaneous clinical tuberculous disease are concerned. WALLGREN, Gothenburg, Sweden.

CUTIS MARMORATA TELANGIECTATICA CONGENITA. H. TONSETH, Norsk mag. f. lægevidensk. **96**:891 (Aug.) 1935.

In 1932 Lohuizen described a peculiar congenital anomaly of the skin, consisting of a general dilatation of the superficial veins, causing a marmorated aspect. He called it cutis marmorata telangiectatica congenita. Tonseth has observed another case of the same congenital disease in a new-born girl. The changes were most pronounced on the head. There were signs of malnutrition of the skin, with oblong areas of necrosis following the direction of the distended veins. The telangiectasis healed, leaving scars. WALLGREN, Gothenburg, Sweden.

Surgery and Orthopedics

EVAPORATION OF WATER FROM SUPERFICIAL BURNS. G. S. MCCLURE, Arch. Surg. **32**:747 (May) 1936.

Experiments were carried out in thirteen cases of first degree and second degree burns to determine if evaporation from burned surfaces accounts for a significant portion of the dehydration of the body that is believed to be present after accidental burns and to determine also if the treatment of these surfaces with tannic acid materially modifies this evaporation. It was found that the rates of evaporation from areas of first degree and second degree burns were increased. Tannic acid formed a hard covering and prevented evaporation in second degree burns. In first degree burns tannic acid did not form a coagulum; consequently evaporation remained high. KAISER, Rochester, N. Y.

THE ACETABULAR INDEX IN INFANTS IN RELATION TO CONGENITAL DISLOCATION OF THE HIP. SAMUEL KLEINBERG and H. S. LIEBERMAN, Arch. Surg. **32**:1049 (June) 1936.

Kleinberg and Lieberman sought a method for recognizing during the early months of life any maldevelopment in the structures of the hip likely to eventuate in dislocation. They studied the angle of inclination of the iliac segment of the acetabulum to the horizontal line in normal and in congenitally dislocated hips, in the hope of obtaining some practical basis of measurement that would help in

determining whether the hips of a new-born infant are normal or are likely to become dislocated. Twenty-three infants whose hips were normal and thirty-five infants with congenitally dislocated hips were examined by means of roentgenograms. It was found that the acetabular index for the hips of new-born normal infants is regularly low and lower at 2 years of age. The acetabular index for congenitally dislocated hips is constantly high. It is concluded that an infant with a high acetabular index should be placed in an apparatus in order to hold the lower limbs continuously in marked abduction.

KAISER, Rochester, N. Y.

SURGICAL TREATMENT OF ANOMALIES OF UPPER URINARY TRACT IN CHILDREN. M. F. CAMPBELL, J. A. M. A. **106**:193 (Jan. 18) 1936.

An anomalous organ is more subject to disease than a normal one, and if anomalies are found in the lower part of the urinary tract the chances are great that the upper urinary tract is anomalous. Most interest is focused on obstructive uropathy, because congenital hydronephrosis and chronic pyuria are found associated with it. Although the recuperative powers of the kidneys of the young favor conservative surgical intervention, delay in the diagnosis of the commoner anomalies of the upper urinary tract often renders nephrectomy necessary. Attention to preoperative preparation, conservation of the body heat, rigid hemostasis and minimal trauma during operation, together with considerate postoperative care, make it possible to care for young patients successfully by radical attack.

BONAR, Salt Lake City.

THE MANAGEMENT OF STRUCTURAL SCOLIOSIS. SAMUEL KLEINBERG, M. Rec. **142**: 536 (Dec. 18) 1935.

The chief objects in the treatment of structural scoliosis are: (1) reduction of the curvature of the spine, (2) improvement of the appearance of the back, (3) diminution of the prominence of the projecting ribs and (4) arrest of the increase of the deformity.

When the maximum amount of improvement has been obtained, it is important to decide how the improvement can be maintained and a relapse avoided. Kleinberg discusses the methods he considers best for continuous improvement and then takes up the operative treatment.

WILLIAMSON, New Orleans.

FOOT DEFECTIVENESS IN SCHOOL CHILDREN. MAURICE J. LEWI, Pub. Health Rep. **51**:631 (May 15) 1936.

This survey was carried out on two hundred and eighty-two school children in New York City, most of whom were colored. The results are given in the table.

Foot Defects in Two Hundred and Eighty-Two School Children

Defect	Percentage	
	Boys	Girls
Improper mode of walking	34	32
Defective posture	37	25
Improper foot-gear	58	61
Superficial defects	33	32
Weak foot	69	57
Functional impairment of the anterior metatarsal arch	32	33
Hallux valgus*	0	33

* Including all minor deflections of the great toe.

SANFORD, Chicago.

VOLKMANN'S SYNDROME. JACQUES LEVEUF, Rev. d'orthop. **23**:5 (Jan.-Feb.) 1936.

This syndrome has two stages: (1) onset with inability to move the muscles of the forearm and the hand, often pain or tingling, edema and cold, cyanosed fingers; (2) retraction of the fingers and hand in "griffe."

The edema is not a true edema due to compression, since it does not disappear rapidly after the removal of the constricting bandages.

The typical *griffe de Volkmann* consists of hyperextension of the proximal phalanx, flexion of the two distal phalanges and flexion of the wrist, with loss of motion of the adductor muscles of the thumb and of the intrinsic muscles of the hand.

In section the muscles are pale, almost cadaverous, and segmented, with prominent Bowman's disk. Many macrophages and multinuclear cells are scattered throughout the sections.

The author expresses the belief that a predisposition within the tissues is necessary for the development of Volkmann's syndrome. His studies have shown the presence of spasmodic contractions in the arteries, arterioles and precapillaries, and it is his belief that such a condition develops only in predisposed tissue.

RYAN, Vancouver, Canada.

ANEMIA AND HYPERPYREXIA AS POSTOPERATIVE COMPLICATIONS IN INFANTS. JAN KOSSAKOWSKI, Pedjatrja polska **15**:110, 1935.

Much has been written in the French and other European literature on anemia and hyperpyrexia in infants as postoperative symptoms often associated with rapid death. Kossakowski discusses extensively the causes of these complications. The most important point to remember is that they occur most frequently in infants under 1 year of age.

The author reports a number of cases in which these complications occurred. Some of the reports have résumés of postmortem examination. No cause of the complications was found. In the surgical department of the Children's Hospital in Warsaw the following rules have been instituted:

1. Operations on infants are postponed until the patients are over 1 year of age, if possible.

2. The infant should stay in the hospital for some time preoperatively or should be brought daily to the clinic for several days before the operation. If there is any suspicion of an infection of the upper respiratory tract the operation is postponed.

3. The prognosis is guarded in all operations on infants.

KRUPINSKI, Chicago.

Teeth and Dentistry

SOME ASPECTS OF DENTAL ARCH GROWTH. SAMUEL J. LEWIS, J. Am. Dent. A. **23**:277 (Feb.) 1936.

A periodic examination, including oral plaster casts, of children studied through the cooperation of the Merrill-Palmer School of Detroit was made. Dr. Lewis presents an analysis of the width of the cuspid in the dental arches of the growing child. His findings indicate that there is some similarity in the dimensional increases in this area for those children in whom a normal functional denture ultimately develops. The amount of growth and the chronological age at which this growth takes place was not uniform. The growth of the intercuspid region is apparently coincidental with the eruption of the permanent incisor and cuspid teeth. One period of accelerated growth, beginning during the eruption of the incisors, and a second less variable period, beginning with the eruption of the permanent cuspids, were noted. Growth of the lower denture normally precedes that of the upper denture and forms the pattern on which the upper denture is

modeled. Periods of adjustment occur during the plateaus when less or no dimensional increase takes place.

Whether the final result is one of normal or abnormal occlusion appears to be allied not only to the relationship of the individual teeth in each arch but to the relationship of the arches and the time of shedding and eruption of the teeth. Dr. Lewis believes that repeated observation is of great assistance in the diagnosis of malocclusion.

NOYES, Chicago.

A STATISTICAL STUDY OF CARIES IN THE DECIDUOUS AND PERMANENT TEETH OF CHILDREN. JOSEPH T. COHEN, J. Am. Dent. A. **23**:312 (Feb.) 1936.

From a study of 2,554 children ranging in age from 2 to 15 years the author has tabulated the incidence of caries with regard to age, sex, race (with respect to Jewish and non-Jewish children) and socio-economic class. His conclusions are that girls have slightly better permanent teeth than do boys up to about 13 years of age. Children from families of higher socio-economic groups have better deciduous teeth but a somewhat higher incidence of caries in the permanent teeth than children of lower socio-economic groups. The deciduous teeth of non-Jewish children are better than those of Jewish children up to the age of 6 years; the conditions are similar thereafter. The permanent teeth of Jewish children seem to be slightly better than those of non-Jewish children after the age of 12. Approximately 80 per cent of the lower first permanent molars were defective by 10 years of age. It should be noted that in the socio-economic classes into which Dr. Cohen divided 1,437 children studied from this standpoint the number who could be considered as privileged children obtaining medical and dietary supervision was relatively small. Both the criteria on which the divisions were made and the manner of grouping may have some effect on the conclusions drawn by the author in this respect.

NOYES, Chicago.

CARE NECESSARY FOR THE FIRST TEETH. M. DECHAUME, Rev. méd.-sociale de l'enf. **3**:6 (March-April) 1935.

Dechaume advises strict care of the first teeth rather than neglect of defects and caries, even though these teeth are temporary. Brushing of the teeth with a dilute solution of sodium bicarbonate should start early after their eruption. Cavities should be filled as they develop. The general nutrition of the child must be watched, especially in regard to vitamins and calcium.

SHAW, Evanston, Ill.

THE MANDIBLE OF CHINESE CHILDREN. H. SAKAI, J. Orient. Med. **24**:22 (Feb.) 1936.

This study comes from the Anatomical Institute, Mukden. Tables of angles and indexes are given, and in the discussion comparisons are made with the findings in Chinese adults.

LESLIE, Evanston, Ill.

Miscellaneous

CLINICAL SPECTROSCOPY IN ARGYROSIS. L. E. GAUL and A. H. STAUD, J. A. M. A. **104**:1387 (May 20) 1935.

Gaul and Staud warn of the dangers of argyrosis from the indiscriminate use of colloidal silver preparations and report seventy such cases. Within the past year they observed fifteen cases in children under 10 years of age in which the condition developed following intranasal applications of argyrol and neosilvol. As there is no treatment for argyria at present, these children will be discolored for life. The degree of discoloration depends on the duration and intensity of solar or artificial radiation. Argyria becomes clinically apparent when

the equivalent of 0.8 Gm. of silver arsphenamine is retained. Analysis by biospectrometric methods affords a new test for the identification of argyria.

BONAR, Salt Lake City.

STUDIES ON THE VENOMS OF NORTH AMERICAN PIT VIPERS. T. S. GITHENS, J. Immunol. **29**:165 (Aug.) 1935.

A study was made of the venoms of more than twenty-five species of North American pit vipers, most of which were different species of rattlesnakes. In general, the amount of venom secreted by each species varied directly with the size of the species. The smaller snakes generally yield more potent venom per unit volume than the larger. However, because of the greater volume of venom yielded by the larger snakes, a single extraction of venom contains a greater number of fatal doses. An analysis of the mortality from snake bites in man indicates that the danger from bites varies almost directly with the size of the species.

FOTHERGILL, Boston.

STUDIES ON THE PHARMACOLOGY OF ETHYL ALCOHOL. O. W. BARLOW, J. Pharmacol. & Exper. Therap. **56**:117 (Feb.) 1936.

The question not infrequently arises as to whether alcohol (ethyl) is as suitable to use, therapeutically by mouth, as whisky. On the basis of the carefully conducted experiments on man, other mammals and lower forms of life reported by Barlow it would seem safe to answer the query in the affirmative; the local action and the toxicity of whisky were somewhat greater than those caused by equivalent doses of alcohol.

PILCHER, Cleveland.

AUTOGENOUS VACCINE THERAPY IN PEDIATRICS. C. J. BLOOM, New Orleans M. & S. J. **88**:738 (June) 1936.

Bloom reports his results with autogenous vaccines in forty-six cases of common cold, thirty-five cases (selected) of bronchial asthma, thirty-three cases of pyelitis and eleven cases of furunculosis. He concludes that in the cases of common cold autogenous vaccines were proved ineffective.

In the cases of asthma the results were much better, with cures in 25.7 per cent and improvement in an additional 40 per cent. The cases of asthma were selected in that all the patients had negative or very mild reactions to food tests and all had had their tonsils removed.

In the thirty-three cases of pyelitis resistant to treatment other than cystoscopy, he obtained good results in 45.5 per cent. The results seemed to be better when more than one organism had been recovered and used in the vaccine.

The eleven patients with furunculosis were all cured.

He concludes that the use of autogenous vaccine is warranted in asthma of bacterial origin, in pyelitis resistant to medical treatment and in furunculosis.

BERKLEY, Los Angeles.

THE DISTRIBUTION AND DIAGNOSTIC SIGNIFICANCE OF LEAD IN THE HUMAN BODY. C. N. MYERS, FLORENCE GUSTAFSON and BINFORD THRONE, New York State J. Med. **35**:579 (June 1) 1935.

The improved methods for estimating the lead content of blood, urine and hair reveal a much higher rate of lead poisoning than has previously been suspected. The cumulative effects of small doses of lead cause, in the authors' opinion, many obscure symptoms which are now being missed by physicians. Various syndromes may be associated with "sub-chronic" lead poisoning. The symptoms are variable and may simulate those of mental disease, acute peritonitis, disease of the gallbladder and renal colic. Early symptoms are anorexia, nausea, weariness, constipation, headache, ocular symptoms and circulatory manifestations. Careful laboratory examinations for lead poisoning should always be considered in the study of obscure cases.

AIKMAN, Rochester, N. Y.

AN UNUSUAL OCCURRENCE OF THALLIUM POISONING: SEVEN MEMBERS OF A FAMILY AFFECTED WITH FIVE FATALITIES, WITH DIAGNOSIS ESTABLISHED BY MEANS OF SPECTROSCOPIC ANALYSIS. J. B. NEAL, E. APPLEBAUM, L. E. GAUL and R. J. MASSELINK, New York State J. Med. **35**:657 (July 1) 1935.

Three deaths in one family were at first considered as due to encephalitis following varicella, but careful investigation brought out the presence of thallium poisoning in three adults and five children. The mother, a boy of 9½ years, a girl of 7 years, a boy of 3½ years and a girl of 1½ years died. Another boy, aged 5 years, recovered after showing alopecia and other signs of thallium poisoning. The diagnosis was confirmed by spectroscopic examination. The article does not mention how the poisoning occurred.

AIKMAN, Rochester, N. Y.

MECHANISM OF METHYLENE BLUE IN CO-POISONING. M. M. BROOKS, Proc. Soc. Exper. Biol. & Med. **34**:48 (Feb.) 1936.

Rabbits were exposed to an environment of carbon monoxide, and the blood was analyzed spectroscopically at various intervals after solution of methylene blue was injected intravenously. The results show that methylene blue changes carbon monoxide-hemoglobin into oxyhemoglobin in the blood stream and not into methemoglobin, as was stated by Henderson. Also, they confirm previous results that methylene blue is an antagonist for carbon monoxide poisoning and acts rapidly.

HANSEN, Minneapolis.

THE MUNICIPAL CHILDREN'S HOSPITAL. AGUSTÍN CASTELLANOS Y GONZÁLEZ, Arch. de med. inf. **4**:45 (June) 1935.

A description of the work done in the City Hospital for Children, Havana, Cuba, is given by the director.

SANFORD, Chicago.

USE OF EMETINE IN PEDIATRICS. CASTRO BARRETO, Lab. clin., Rio de Janeiro **15**:227 (Aug.) 1935.

Emetine chloride disturbs the cardiac rhythm and in cases of intoxication may cause death. Three cases of severe dysentery in children are cited, in which this drug was not used. Complete recovery occurred. Barreto believes that care should be used in the administration of this drug.

SANFORD, Chicago.

CLINICAL CONCEPTION OF INFANTILISM. BAUDILIO DANES, Paidoterapia **14**:123 (June) 1935.

Infantilism is a suspension of development during childhood. The diagnostic characteristics are as follows: The general morphologic features of the body and the various proportions of the component parts, as well as the state of development of the genital apparatus and the mental development, are of the infantile type. All these exist together, without any exception. A historical résumé of this malady is given.

HERRON, Spokane, Wash.

BLOOD TRANSFUSION IN CHILDHOOD. HANS KNAUER, Arch. f. Kinderh. (supp.) **7**:1, 1936.

The results of several thousand transfusions in children give convincing evidence of the value of the procedure. The indirect method of the intravenous injection of citrated blood is easily carried out, and with the usual precautions there is no danger of undesirable results. Transfusion is effective not only for anemias but for a great variety of conditions, including especially infections, against which it helps to build up immunity.

CRANE, Chicago.

So-Called Idiosyncrasies in Infancy. Ludwig Seitz, Monatschr. f. Kinderh. **63**:310, 1935.

Two cases of idiosyncrasy to food are reported in children. The first infant reacted severely, with nausea, vomiting, diarrhea, fever and extreme pallor, to a mixture of buttermilk containing rice gruel. Various tests were made, and it was concluded that without question the condition was an allergic reaction to cow's milk. However, passive transfer tests gave negative results. In the second case there was a cutaneous reaction following the eating of shell-fish. In both cases the treatment consisted of desensitization with small quantities of the food by mouth. In the second case associated eczema also improved under the treatment.

Gerstley, Chicago.

Silver Staining of Stippled Red Cells in Lead Poisoning. M. Nagahama, J. Pediat. (Tokyo), no. 429, Feb. 20, 1936, p. 294.

The erythrocytes of the blood from patients with lead poisoning are washed in physiologic solution of sodium chloride and fixed in Champy's fluid. After repeated washing and centrifugation, the cells are mixed with 2 per cent gelatin and 2 per cent hydroquinone solution and washed. Then a 2 per cent solution of silver nitrate in 2 per cent gelatin is added and the mixture heated at 65 C. for four minutes; the preparation is next washed in water several times by centrifugation. Then it is treated with a 1 per cent sodium hyposulfite solution for one minute and washed. A loopful of the cells is then spread on a slide, air-dried, sealed in xylene-balsam and examined under the oil immersion lens. In lead poisoning the silver-stained granules appear as coarsely reticular, granular or linear bodies, while in normal blood there are only very fine granules.

Kato, Chicago.

Respiration and Basal Metabolism in Childhood During Sleep. M. de Bruin, Acta pædiat. **18**:279, 1936.

The metabolism, as well as the rate and amplitude of respiration, of twenty-two normal children was measured both under basal conditions and during sleep. The author draws the following conclusions: In children the respiratory volume per minute is lowered during sleep; the decrease does not usually exceed 25 per cent of the volume of air breathed per minute while the subject is awake. The decrease in minute volume is produced chiefly by slowing of the rate of respiration. The rate of metabolism is lowered soon after the beginning of sleep; the decrease in metabolism is less conspicuous than the change in volume of respired air.

McCune, New York.

Society Transactions

NEW YORK ACADEMY OF MEDICINE, SECTION OF PEDIATRICS AND SECTION OF SURGERY

April 3, 1936

BÉLA SCHICK, M.D., *Chairman*

ALEXANDER T. MARTIN, M.D., *Secretary*

INSTANCES OF ANOMALOUS STRUCTURE AND DERANGEMENT OF FUNCTION OF THE GASTRO-INTESTINAL SYSTEM IN CHILDREN (LANTERN SLIDE DEMONSTRATION). DR. CHARLES GILMORE KERLEY.

In my discussion of the nonsurgical aspects of gastro-intestinal disorders I shall first call attention to a world-wide childhood complaint of anorexia.

Habitual loss of appetite in an otherwise healthy child, it has been demonstrated in a vast number of cases, is due to a stomach content of food residue or mucus or both in considerable amounts four hours or longer after feeding. For appetite in a child there must be an empty stomach. A stomach content is readily demonstrated by the use of a stomach tube four hours after the completion of a meal. Lantern slides are shown, demonstrating the stomach contents found in children whose only complaint was persistent anorexia. Among those shown is that of a boy 18 months of age who was brought for examination because of habitual refusal of food; he had eaten but little the day before; 2 ounces (56 Gm.) of milk and cereal had been forced into him at 8 a. m.; he arrived at my office at 1 p. m. Examination of the stomach by means of a tube revealed a content of 5 ounces (142 Gm.) of residue five hours after the completion of the morning meal, which means that 3 ounces (85 Gm.) was a carry-over from the previous day. The findings are characteristic of a vast number of others with the complaint of habitual absence of appetite.

The cause of the delayed emptying usually proves to be either pylorospasm or plugging of the pyloric orifice with a thick mucus content. The further demonstration consists of roentgen studies of the gastro-intestinal tract in persistent digestive disorders.

The benefit of a roentgen serial including the barium sulfate enema was given 434 patients with persistent gastro-intestinal disorders. In the study of 27 of the patients additional roentgenograms of the stomach were taken. For the sake of brevity I have divided the patients into groups according to the outstanding clinical symptoms and shall demonstrate the roentgen findings peculiar to the several groups.

Colic.—The outstanding complaint concerned severe paroxysmal abdominal pain extending over several months or years. Otherwise the children as a rule enjoyed average good health. Lantern slides are shown demonstrating the findings in these patients, which consisted in a regional spasm of the circular muscle fibers at the pyloric orifice of the stomach and active pylorospasm or a regional spasm of the circular fibers at different points of the large intestines, with resulting gas block and hyperperistalsis. In the majority of the cases these conditions were found in the so-called spasmophilic child. It has been possible to demonstrate this phenomenon of incoordination only in the stomach and large intestines. It has been possible to take roentgenograms of the patients under the throes of the colic—slides are shown demonstrating the localized areas of spasm during the attack.

Conditions of this sort usually represent careless and irrational feeding; they are very readily relieved by a properly arranged three meal a day diet with absence of fruit juices before breakfast and giving of iced foods only after meals. Mineral

oil is useful in regulating the intestinal function, and administration of atropine in nearly physiologic doses is carried out for a considerable period of time in all.

Recurrent Vomiting.—The histories reveal repeated attacks of severe vomiting lasting from one to three days. The patients were usually undersized and underweight. The outstanding roentgen observation was that the colon was highly spastic. Two cases were demonstrated in slides showing retention of barium sulfate in the spastic colon for seventy-two hours. In one there was an associated spasm of the sphincter ani. In several instances chronic appendicitis afforded the explanation of the colonic spasm.

The immediate treatment for such recurrent attacks is hypodermic injection of codeine phosphate, from ¼ to ½ grain (0.016 to 0.032 Gm.), usually with atropine from $\frac{1}{150}$ to $\frac{1}{200}$ grain (0.0004 to 0.0003 Gm.), repeated if required.

Intestinal Stasis.—This group includes the greatest number of the patients. The children showed a wide range of gastro-intestinal complaints, prominent among which were loss of appetite, vague abdominal discomfort, slight persistent elevation of the temperature, moderate malnutrition, secondary anemia and habitual constipation. Rarely, if ever, an evacuation occurred without a laxative or an enema having been given. Lantern slides are shown of a boy and a girl of 7 years in whom, the parents insisted, there never had been a normal unassisted evacuation. These slides show both anatomic and functional derangement. Almost all the patients had ptosis of the colon, and some, gastroptosis; usually there was a greatly elongated and redundant colon and sigmoid. Localized spasm of circular fibers was also frequent; a dilated cecum was not infrequently found as an associated anomaly.

In all cases of this type a Bassler belt is fashioned to fit the child. Mineral oil, given two or three times a week, a diet containing roughage, and the aromatic fluidextract of cascara sagrada U. S. P., in small doses three times a day, are sufficient to take care of the intestinal stasis.

Persistent Malnutrition.—Persistent malnutrition in its relation to gastro-intestinal mechanics has received strikingly little attention. Many children are brought for examination because of faulty growth and delayed general development. The story is that of lack of appetite, habitual constipation and habitual medication with laxatives. The child is usually a poor sleeper, habitually unhappy, poorly resistant; he suffers from cold hands and feet during the winter; his school work is poor; he does not get along well with other members of the family—he is of the antisocial type; he is invariably underweight and usually underheight for his age. Examination of the vital organs, the endocrine system, the basal metabolism, the blood pressure and the bone age fails to reveal a cause for the malnutrition. Tests for tuberculosis and syphilis prove negative. There is usually more or less lordosis with the accompanying "pot belly." Several lantern slides demonstrating the gastro-intestinal findings in such children are presented. These poor physical specimens may have their bodily secrets revealed by the roentgen rays. A slide of the gastro-intestinal tract of a 12 year old girl typifies what was found in this group: extreme gastro-intestinal ptosis—a considerable portion of the stomach being below the level of the iliac crest, the colon being entirely below this level and the apex of the triangle formed by the prolapsed colon extending in a V-shaped formation deep into the pelvis until it is at a level with the pubic symphysis.

The management consists in using the Bassler belt with shoulder support, requiring the child to sleep on a hard mattress with a flat pillow—better, none—and applying other measures along the lines indicated by the nature and degree of the physical deficiencies.

ACUTE MESENTERIC LYMPHADENITIS SIMULATING ACUTE APPENDICITIS. DR. HENRY W. CAVE.

At the Roosevelt Hospital, during a period of five years, an effort has been made to differentiate properly the symptoms, signs and laboratory findings of

acute appendicitis from those of acute mesenteric lymphadenitis. An analysis of the data on 21 patients who were subjected to operation has been made.

The months of late fall, winter and early spring show generally an increase in the incidence. This is in keeping with the occurrence, particularly in children, of infections of the upper respiratory tract, although there are months in summer when gastro-enteritis from infected food, heat and dietary disorders is a causative factor. More males are affected than females. The mode of infection is not clearly understood. Infected nasal and throat secretions and contaminated water, milk and food find their way to the lower end of the small bowel; the pathogenic bacteria here invade and pass through the intestinal wall by way of lymph channels into the neighboring nodes. Concurrent sore throat or coryza was observed in 40 per cent of the patients. The pain is colicky; there are intermittent paroxysms, which in the minds of some investigators are indicative of lymphadenitis. In acute mesenteric lymphadenitis pain and tenderness are certainly more generalized than in acute appendicitis, and rigidity is a variable finding. If present, it is usually mild or moderate and is demonstrable over a more extensive area than in acute appendicitis. Distention is rarely encountered. Palpable masses may at times be outlined.

We have been struck by the fact that there are many cases of acute appendicitis in which the lymph nodes are enlarged, and from the pathologic reports on many of the cases in which appendixes were removed we are not so sure that there is a distinct clinical entity which can be termed "acute lymphadenitis." In other words, it may be that disorders of the appendix cause swelling and inflammation of the ileocecal lymph nodes. The disease is not prolonged; in many of our cases it lasted only a few days; after operation the course of the symptoms and signs terminates quickly. Great emphasis is placed on the fact that it is dangerous to remove a swollen lymph node at the time of the operation; it is naturally well to remove the appendix.

If one is in doubt as to the progress of the disease, it is far wiser to explore and remove a normal appendix than to wait and court disaster from one that has ruptured.

HIRSCHSPRUNG'S DISEASE. DR. EDWARD W. PETERSON.

Cases of congenital idiopathic dilatation of the colon (megacolon congenitum) had been recorded before Hirschsprung in 1886 described in more detail the disease which has since borne his name as "a condition of congenital high grade dilatation of the colon, with thickening of all its tunics, especially the tunica muscularis, and retention of large quantities of fecal matter."

Etiology.—The cause of the congenital tendency of the colon to dilate is unknown. The dilatation is much more frequent in boys than in girls. That it is congenital is indicated by the characteristic picture appearing at or shortly after birth. Ladd found it in a 7 month fetus. It seems probable that the underlying factor is neurogenic, for definite neuromuscular imbalance and dysfunction are present, and the colon seems incapable of emptying itself of the large fecal accumulations. As Adson pointed out, the mechanism for filling the colon and sigmoid is more powerful than the emptying mechanism and overbalances it. The sympathetic outflow of inhibitory muscular stimuli to the colon and the contracting stimuli to the internal sphincter of the rectum are more powerful than the parasympathetic motor stimuli to the musculature of the colon and the inhibitory stimuli to the internal sphincter of the anus. Defective parasympathetic innervation would produce a similar effect, since the emptying would be less than the filling and retaining stimuli.

Pathologic Anatomy.—The dilatation and hypertrophy usually involve the sigmoid, but the whole of the large intestine and even the appendix may be affected. There is also elongation of the large bowel, especially of the sigmoid flexure. The mesocolon may also be longer than normal. In cases of long standing, inflammatory changes, even ulceration, may develop.

Symptoms.—The cardinal symptoms are dilatation of the colon, abdominal distention and obstinate constipation. Often there is languor, apathy, loss of weight, anemia and general muscular weakness. Occasionally there may be abdominal discomfort, vomiting, fever and evidences of autointoxication. When diarrhea occurs, it suggests irritation or ulceration of the colon and is usually merely the overflow of fecal retention.

Course and Prognosis.—The prognosis of congenital idiopathic dilatation of the colon is unfavorable. Most of the patients die of increasing inanition and debility or of some complication such as bronchopneumonia, cardiac failure, nephritis, chronic intestinal toxemia and, rarely, peritonitis from perforation. The patients who reach adult age are for the most part chronic invalids.

Diagnosis.—Dilatation of the colon, abdominal distention and obstipation in an infant or child in the absence of any demonstrable evidence of organic obstruction to the bowel is sufficient basis for a diagnosis of Hirschsprung's disease.

Treatment.—Up to ten years ago, the results from both medical and surgical treatment proved disappointing. The high mortality and morbidity following surgical operations such as ileocolostomy, cecostomy, colon resections, etc., were so discouraging that surgeons were reluctant to operate in these cases. During the past ten years, however, lumbar sympathetic neurectomy has given such satisfactory results that it is now the method of choice in the treatment of Hirschsprung's disease.

Historically, it is of interest to recall that it is to Royle, an orthopedic surgeon, and to the late John Hunter, an anatomist, both of Sidney, Australia, that credit is due for the revival of and continued interest in the surgery of the sympathetic nervous system. Royle attempted to relieve the spasticity or rigidity following war wounds of the central nervous system and reported encouraging results following lumbar sympathetic ganglionectomy. Unfortunately this promise of benefit was not confirmed by many other workers in this field. Two interesting observations, however, resulted from this work: (1) the capillary circulation was increased and the temperature of the skin was permanently elevated in a sympathectomized limb, and (2) obstinate constipation was relieved in selected cases.

Applying this knowledge, Adson, at the Mayo Clinic, in March 1925, operated on a patient with Raynaud's disease of the lower extremities. In 1926 Wade and Royle operated on a patient with Hirschsprung's disease, doing a lumbar sympathetic ramisection, with an excellent result. Since the report of this case, Adson, Judd, Rankin and Learmouth, all of the Mayo Clinic, Wade, Scott and other surgeons in this country and abroad have given encouraging accounts of their experience with this operation.

The method proposed by Wade, the original operator, was extraperitoneal division of the paravertebral sympathetic cord below the fourth ganglion, with division of all medially directed rami up to the level of the inferior mesenteric artery, through a long incision in the flank. Adson and Judd advocated a transverse abdominal approach and bilateral ganglionectomy of the second, third and fourth lumbar ganglions. Very recently Adson has advised, in addition to bilateral ganglionectomy, wide resection of the superior hypogastric plexus or of the presacral nerves, including all sympathetic fibers from the lumbar chain, all intermesenteric fibers descending into the pelvis, below the inferior mesenteric artery, and those fibers which rejoin the hypogastric plexus from the inferior mesenteric nerve in the mesocolon of the pelvis.

My own experience in this field is limited to operation in 4 cases of Hirschsprung's disease. The results in all of them have been gratifying. However, careful supervision over the patients must be maintained for an indefinite period; otherwise relapses will take place. Bowel habits, diet, exercise, etc., should be regulated carefully in each case. As has been pointed out, the operation corrects the physiology by causing a break in the hyperactive inhibitory control of the bowel, but it does not correct the pathologic anatomy.

The treatment of idiopathic dilatation of the colon by medical means has always proved unsatisfactory. Colon resections and short-circuiting operations,

too, not only have a prohibitive mortality but often have shown disappointing functional and symptomatic end-results. Dr. Edward J. Donovan on one or two occasions has performed lumbar sympathectomy successfully after failure of radical resection of the colon to effect a cure. Dr. Charles L. Janssen has given warning that not all of the results have been as gratifying as the published ones. Dr. A. A. Berg believes that the elongation of the colon with the ever-present danger of volvulus calls for resection of the sigmoid in addition to sympathetic neurectomy. Dr. Frank L. Meleney reported failure of resection of the left lumbar sympathetic cord and later right ganglionectomy. Finally an anastomosis between the cecum and the distal portion of the sigmoid was effected, with resection of the dilated bowel from the proximal portion of the transverse colon to the distal part of the sigmoid. This radical procedure was followed by a symptomatic cure.

Lumbar sympathetic neurectomy has proved successful in the experience of so many surgeons throughout the world that in spite of occasional poor results it should be considered the method of choice in the treatment of selected patients with congenital idiopathic dilatation of the colon.

Book Reviews

Die Leukosen im Kindesalter. By Dr. Heinrich Willi. Price, 7.35 marks. Pp. 205, with 26 illustrations. Berlin: Karger, 1936.

This monograph presents a comprehensive discussion of the clinical and hematologic problems offered by leukemia (the leukoses) in children. The discussion is based on the histories of 50 cases of leukosis observed by the author and of 492 cases reported in the literature. The author follows Nägeli's concept of the dual nature of the disease and considers the lymphadenoses and myeloses. He differs from Nägeli on a few points of hematologic interest. Nägeli expressed the belief that blood cells are derived from the primitive mesenchyme cell, which produces the proerythroblast, the lymphoblast and the myeloblast, and that these forms are the forerunners of the mature elements of the blood. He stated that granular leukocytes, monocytes and megakaryocytes are derived from the myeloblast. He was of the opinion that in leukemia the myeloblast may produce a pathologic cell, the paramyeloblast, which is the common cell of leukemia. Analogous to the paramyeloblast is the paralymphoblast, which is present in lymphoid tissue in the leukemic state. The author feels that the paramyeloblast is not a pathologic cell typical of leukemia but is a normal constituent of the bone marrow, which increases in other disorders of the bone marrow, such as agranulocytosis and sepsis.

The author classifies the leukoses according to the predominating cell type, as follows:

I. Lymphadenoses
   - A. Lymphoblastic (paralymphoblastic)
   - B. Lymphocytic
   - C. Characterized by plasma cells

II. Myeloses
   - A. Myeloblastic (paramyeloblastic)
   - B. Promyelocytic
   - C. Myelocytic
   - D. Eosinophilic
   - E. Monocytic

He classifies the conditions clinically, according to the cardinal symptoms presented by each patient, as follows:

I. Lymphadenoses
   - A. Anemia
   - B. Hemorrhagic diathesis
   - C. Ulceration of the pharynx
   - D. Generalized enlargement of the lymph nodes
   - E. Mikulicz' syndrome
   - F. Bony overgrowth—chloroma
   - G. Lesions of the central nervous system
   - H. Cutaneous infiltration

II. Myeloses
   - A. Splenomegaly
   - B. Formation of tumors
   - C. Septic picture

These clinical types are freely illustrated by concise histories and by graphs chosen from the data on the author's cases. Especially interesting are the cases in which anemia was the outstanding symptom. He found that sternal puncture was of value in such cases in differentiating the condition from aplastic anemia.

The discussion of the differential diagnosis is excellent, although it is evident that the crux of the problem will remain unsolved until better methods for cytologic technic are developed. Clinical aids in the diagnosis of lymphadenosis are (1) the greater frequency of lymphadenosis in childhood except during the first year of life, when the myeloses are more common; (2) the tendency to tumor formation, and (3) the hematologic features. The author admits the difficulty in differentiating immature basophilic round cells but states that the lymphoblast

can be distinguished from the myeloblast in properly prepared smears. The pathologic cell of lymphatic leukemia varies in size, being from one to four times that of the erythrocyte, is round or oval and has a narrow rim of cytoplasm, which appears at times to be absent (*naktkernig Foramen*). The nucleus has a thin irregular nuclear wall, a leptochromatic structure with from one to three nucleoli. This cell differs from the lymphoblast in the relatively larger polymorphic nucleus. This is the paralymphoblast of Nägeli. The author differentiates the lymphoblast from the myeloblast chiefly by (1) the structure of the nucleus and (2) the total cell composition of the smear or section. He points out that in lymphadenosis normal lymphoblasts and lymphocytes are usually present and immature myeloid or granular forms absent, while in myelosis mature neutrophils and usually a few transition forms are present among the paramyeloblasts. He expresses the opinion that the *hiatus leucemicus* of Nägeli (a term descriptive of the usual finding of large numbers of myeloblasts and many mature neutrophils without transition forms) is not a constant finding and that a few transition forms, which aid in identifying the immature cell type, are usually present. The pathologic picture of lymphadenosis may be obscured by a terminal infection which produces a myeloid response, but as a rule the picture is typical.

The author is of the opinion that the only positive indication as to the etiology of the condition lies in the predisposing factor of antecedent infection. He states that roentgen therapy is the only helpful therapeutic aid and that this is contraindicated in cases of acute involvement.

La vie sexuelle de la femme. By André Binet. Price, Paris, 40 francs; France, 44 francs. Pp. 355, with 72 illustrations. Paris: L'Expansion Scientifique Francaise, 1937.

This small manual begins with a simple outline of the anatomic and psychic changes which occur during the growth of the child from infancy to adult life. The appearance and the development of the secondary sexual characteristics and the psychic evolution of puberty occupy two brief chapters. A brief discussion, almost an outline, is given of the influence of the various endocrine glands on the changes incident to maturity. Nothing new is presented.

In Part II the sexual life of the adult woman is discussed. The influence of the various endocrine substances is described briefly. The facts stated are accurate and clearly given. The reproductive cycle is discussed in a brief and summary manner, in three short chapters. Disorders of menstruation occupy one chapter. The brief discussions of the abnormalities of menstruation are commendable, but one scarcely agrees with the author's opinion of the value of savin, apiol, yohimbine and similar drugs for the treatment of amenorrhea. The majority of American gynecologists, also, would scarcely favor dilation of the cervix as a treatment of this condition, nor would they be inclined to ascribe much influence to anteflexion as a cause. In the treatment of uterine hemorrhage, also, they would place less value on drug therapy than does the author. One is surprised that the intramuscular use of estrogen-containing preparations is not suggested for some forms of functional bleeding.

An outline of pelvic anatomy is given, and to this is joined a brief discussion of disturbances of muscular function, or vaginismus. An outline of the anatomy of the blood supply and innervation of the pelvis is followed by a discussion of pelvic pain, which is clear and comprehensive and which would be useful to the student.

One can scarcely agree with the recommendation of the cervical stomatoplasty of Pozzi, which belongs to a class of procedures long since obsolete in this country. Again one wonders why hormonal therapy is not mentioned.

Pelvic pains of various kinds, sterility, fecundation and nidation of the egg and frigidity are discussed in outline form, accurately but without adding to the facts already known.

The little volume gives in outline form a review of the anatomy and physiology of the female pelvis together with a discussion of the management of some of the functional disorders. It will be useful to the student and the practitioner who read French easily and who wish a brief statement of essential facts. The author's reliance on drug therapy seems greater than that found in clinics in this country.

Heilpaedagogische Praxis: Methoden und Material. By Helene Loew-Beer and Milan Morgenstern. Price, paper, 12 shillings; cloth, 14 shillings. Pp. 174, with 71 illustrations. Vienna: Sensen-Verlag, 1936.

This handy volume embraces a discussion of mentally deficient children from the point of view of the limitation of their facilities for expressing whatever ability they possess. A diagnosis of mental deficiency usually spells hopelessness and despair to the relatives and only too often results in abandonment of the effort to help the child utilize his natural possibilities. Contrary to popular belief, the mentally deficient child is generally not lacking in hope, in pride or in similar qualities that bring happiness to the human being.

In this book the authors describe some experiences in an institution for the feebleminded in Vienna, the pedagogic methods employed and the results obtained. A feeling of uselessness and indifference to the tasks assigned was uniformly felt by the children on entrance to the home. Uniform, too, were the successes obtained after tedious but persistent educational maneuvering in an effort to instil confidence in the pupils. Unsuspected talents in certain limited fields are not rarely discovered among seemingly hopeless youngsters. An attribute common to all is happiness in a task done well enough to merit praise and approval.

There is an excellent description of the methods employed, which stress the use of the psychologic principles underlying the processes of learning, repetition, conditioning and imitation. Various mechanical contrivances are described which are utilized in improving muscular coordination. Lessons are illustrated by detailed case records. This book will be of great practical value to persons engaged in teaching subnormal or mentally deficient children. To the pediatrician it offers a bit of encouraging information for his use in dealing with this discouraging class of patients.

The Patient and the Weather. Volume 1, Part II. By Dr. William F. Petersen. Price, $9. Pp. 781, with 366 illustrations. Ann Arbor, Mich.: Edwards Brothers, Inc., 1936.

This is the first volume of the series "The Patient and the Weather," its publication having been delayed in order that certain meteorological data might be checked. Reviews of other volumes have already appeared in this journal. One volume had to do with the chemical and vascular changes which occur in the autonomically unstable person in response to sudden variations in meteorological conditions; another, with the incidence of certain types of disease in the storm tracks of the United States as compared with their incidence in other areas.

This volume has to do with the chemical and vascular response of normal persons to atmospheric changes. The studies were carried out in Chicago, where rapid shifts in temperature, humidity and barometric pressure occur. Of normal men, those of the pyknic type show the greatest stability, adjusting themselves readily to change. The leptosome responds with great swings, which are frequently associated with marked vascular spasm. The response of women is complicated by the changes produced by the menstrual cycle; for example, a sudden increase in barometric pressure aggravates the alkalosis and spasm of the postmenstrual period. Some studies of children are also presented, showing that an increase in restlessness and irritability accompanies pressure episodes.

The point of view and the material are valuable as a balance to the tendency to consider bacteria as the all important feature in disease. Anoxemia of the tissues produced by vascular spasm in association with a chemical shift is undoubtably a factor of great importance. The author deserves considerable credit for his painstaking studies and presentation.

Orthopedic Surgery. By Walter Mercer, M.D. Second edition. Price, $10.00. Pp. 906, with 408 illustrations. Baltimore: William Wood & Company, 1936.

This practical treatise on orthopedics is easy and attractive reading not only because of the content and its illustrations, drawing and photographs, but because its type is large and cleancut and the paper good.

In the individual chapters congenital deformities and general diseases of the skeleton and joints are considered. Particular attention is given to the spine, shoulders, knees and feet, conditions of the nerves manifested in disabilities of the voluntary muscles, complications due to trauma, manipulative surgery, arthrodesis and arthroplasty. Each subject is well illustrated with photographs and drawings. An innovation as far as orthopedic texts is concerned, which is a valuable addition for the physician, is the simple concise discussion of the generally accepted treatment of the various conditions.

The editor and the publishers are to be congratulated on the issuance of this valuable text. It offers a complete and comprehensive presentation of orthopedic surgery and will be appreciated not only by orthopedic surgeons but by other surgeons, by students and by physicians.

Ernährung und Behandlung des Kindes. By Prof. Dr. Erich Müller. Price, paper, 16.60 marks; bound, 18.60 marks. Pp. 600. Stuttgart: Ferdinand Enke, 1936.

This is a short text but a good one on the nourishment and treatment of the child. The first 108 pages are taken up with nutrition, the next 442 with a consideration of general diseases and the last 40 with a description of the measures used in the treatment of children and also in the preparation of various food mixtures. The book is condensed but completely done. In the section on the treatment of diseases, the general characteristics of the diseases are given in fine print and the treatment in larger print. These are not described in detail.

This book gives one a chance to review rapidly any subject which one wishes, and at the same time it states the special points of practically every rare condition which one might encounter.

Applied Dietetics. By Frances Stern. Price, $3.50. Pp. 263, with 52 tables. Baltimore: Williams & Wilkins Company, 1936.

The first hundred pages of this book are devoted to the principles of nutrition, the planning of a diet and the methods and materials helpful in the education of the patient. The last part consists of typical diets and menus containing the foods necessary to supply the food constituents required for the normal diet and of variations in therapeutic diets. The part on the principles of nutrition is well written and easy to read. Enough cannot be said for the tables of diets. Diets of every sort, to meet any kind of an emergency, are given. These are well constructed, containing not only the usual grams and calories but the exact measure in household equivalents. The book is well bound and printed and makes an excellent addition to the subject of dietetics.

Skin Diseases in Children. By George M. MacKee, M.D., and Anthony C. Cipollaro, M.D. Price, $5.50. Pp. 333, with 153 illustrations. New York: Paul B. Hoeber, Inc., 1936.

This small book on cutaneous diseases has been kept to its present size largely by the fact that no account of the pathology of the various diseases discussed is given. For a book on cutaneous diseases this omission is probably permissible.

The book is well illustrated but has no colored cuts, and in view of the present state of color photography in publication this is a serious defect for any book on cutaneous diseases.

The book is short, compact and well written, and the author discusses treatment fairly well. Numerous prescriptions are given. On the whole, the book should prove useful to the general practitioner and to the pediatrician.

Raquitismo en la infancia. Dr. Enrique Sujoy. Paper. Pp. 268, with 90 illustrations. Buenos Aires: Published by the author, 1936.

This book written in Spanish states the history, pathology, etiology, symptoms and treatment of rickets. The chapters on pathology are particularly good, because the chemical findings are completely described and the plates of the microscopic anatomy are clear and well chosen. This is a very good monograph on rickets.

Directory of Pediatric Societies

INTERNATIONAL

International Association of Preventive Pediatrics

President: Professor G. Scheltema, 6a Herreplein, Groningen, Netherlands.
Secretary: Dr. Daniel Oltramare, 15 Rue Lévrier, Geneva, Switzerland.

International Congress of Pediatrics

President: Prof. Luigi Spolverini, Policlinico Lungo Tevere Melini, 24, Rome, Italy.
Secretary: Professor Vitetti, Rome Italy.
Place: Rome, Italy. Time: Sept. 27-30, 1937.

American Committee:
Chairman: Dr. Henry F. Helmholz, Mayo Clinic, Rochester, Minn.
Secretary: Dr. L. Emmett Holt Jr., Johns Hopkins Hosp., Baltimore.

International Congress for the Protection of Children

Secretary: Prof. G. B. Allaria, Corso Bramante 29, Torino 120, Italy.
Place: Rome, Italy. Time: Oct. 4-8, 1937.

FOREIGN

British Paediatric Association

President: Dr. Leonard Findlay, 14 Wimpole St., London, W. 1.
Secretary: Dr. Arthur G. Maitland Jones, 31A Weymouth St., London, W. 1.

Royal Society of Medicine, Section for the Study of Disease in Children

President: Sir Lancelot Barrington-Ward, 85 Harley St., London, W. 1.
Secretary: Dr. K. H. Tallerman, 122 Harley St., London, W. 1.
Place: 1 Wimpole St., London. Time: Fourth Friday of each month, 4:30 p. m.

Paediatrický Spolok na Slovensku

President: Dr. A. J. Chura, Lazaretská 6, Bratislava, Czechoslovakia.
Secretary: Dr. S. Limbacher, Dlhá 2, Bratislava, Czechoslovakia.
Place: Pediatric Clinic, University, Bratislava. Time: Six times a year.

Sociedad Cubana de Pediatría

President: Prof. Félix Hurtado Galtés, Carlos III, 7, Havana.
Secretary: Dr. Carlos Hernández Miyares, San Lazaro 370, Havana.
Place: Cátedra de Clínica Infantil, Hospital Mercedes, Havana. Time: Third Thursday of every month.

Palestine Jewish Medical Association, Section of Physicians of Children's Diseases

President: Prof. S. Rosenbaum, 26 Bialikstr., Tel Aviv, Palestine.
Secretary: Dr. A. Brünn, 9 Maazestre, Tel Aviv, Palestine.

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* Secretaries of societies are requested to furnish the information necessary to make this list complete and to keep it up to date.

NATIONAL

American Medical Association, Scientific Assembly, Section on Diseases of Children

Chairman: Dr. Ralph M. Tyson, 255 S. 17th St., Philadelphia.
Secretary: Dr. Albert D. Kaiser, 16 N. Goodman St., Rochester, N. Y.
Place: Atlantic City, N. J. Time: June 7-11, 1937.

American Academy of Pediatrics

President: Dr. Laurence R. DeBuys, 1417 Delachaise St., New Orleans, La.
Secretary: Dr. C. G. Grulee, 636 Church St., Evanston, Ill.
Place: Waldorf-Astoria Hotel, New York. Time: June 3, 4 and 5, 1937.
Region I. Place: Boston, Mass. Time: Nov. 12-13, 1937.

American Hospital Association, Children's Hospital Section

President: Mr. Robert Witham, Children's Hospital, Denver.
Secretary: Miss Agnes O'Roke, Kosair Crippled Children's Hospital, Louisville, Ky.

American Pediatric Society

President: Dr. Henry F. Helmholz, Mayo Clinic, Rochester, Minn.
Secretary-Treasurer: Dr. Hugh McCulloch, 325 N. Euclid St., St. Louis.
Place: University, Va. Time: April 29-30 and May 1, 1937.

Canadian Society for the Study of Diseases of Children

President: Dr. A. P. Hart, 1844 Bloor St., W., Toronto, Ont.
Secretary-Treasurer: Dr. Pearl Summerfeldt, Hospital for Sick Children, Toronto, Ont.

Society for Pediatric Research

President: Dr. Francis Scott Smyth, University of California Medical School, San Francisco.
Secretary: Dr. A. A. Weech, 3975 Broadway, New York.

SECTIONAL

North Pacific Pediatric Society

President: Dr. L. Howard Smith, 1020 S. W. Taylor St., Portland, Ore.
Secretary: Dr. Morris Bridgeman, Children's Clinic, Portland, Ore.

Southern Medical Association, Section of Pediatrics

Chairman: Dr. Gilbert Levy, 20 S. Dunlap St., Memphis, Tenn.
Secretary: Dr. Hughes Kennedy Jr., Highland Plaza Apts., Birmingham, Ala.

STATE

Alabama Pediatric Society

President: Dr. J. W. Britton, 931 Noble St., Anniston.
Secretary-Treasurer: Dr. Wallace Clyde, Employees' Hospital, Fairfield.

Arkansas State Pediatric Association

Chairman: Dr. A. C. Kirby, 701 Main St., Little Rock.
Secretary: Dr. Madeline M. Melson, 909 Main St., Little Rock.

California State Medical Society, Section on Pediatrics

Chairman: Dr. Edward B. Shaw, 384 Post St., San Francisco.
Secretary: Dr. E. Earl Moody, 3780 Wilshire Blvd., Los Angeles.

Florida State Pediatric Society

President: Dr. Luther W. Holloway, 117 W. Duval St., Jacksonville.
Secretary: Dr. Warren W. Quillian, 227 Avenue Aragon, Miami.
Place: Concurrent with state association meeting at time of convention.

Georgia Pediatric Society

President: Dr. Mercer Blanchard, 1301 Broadway, Columbus.
Secretary-Treasurer: Dr. Don F. Cathcart, 478 Peachtree St., N. E., Atlanta.

Indiana State Pediatric Society

President: Dr. Ernest R. Carlo, 2902 Fairfield Ave., Fort Wayne.
Secretary-Treasurer: Dr. Mathew Winters, 23 E. Ohio St., Indianapolis.
Time: Two meetings a year.

Louisiana State Pediatric Society

President: Dr. Edwin A. Socola, 2000 Tulane Ave., New Orleans.
Secretary-Treasurer: Dr. Ruth Aleman, 1407 S. Carrollton Ave., New Orleans.

Medical Society of State of New York, Section on Pediatrics

Chairman: Dr. George M. Retan, 459 James St., Syracuse.
Secretary: Dr. John D. Craig, 33 E. 61st St., New York.

Michigan State Medical Society, Pediatric Section

Chairman: Dr. Edgar E. Martmer, 749 David Whitney Bldg., Detroit.
Secretary: Dr. C. R. Dengler, 131 W. Michigan Ave., Jackson.

Mississippi State Pediatric Society

President: Dr. Harvey F. Garrison, 319 E. Capitol Pl., Jackson.
Secretary-Treasurer: Dr. Guy C. Jarratt, 920 Crawford St., Vicksburg.
Place: To be designated by Society. Time: Yearly.

Nebraska Pediatric Society

President: Dr. J. A. Henske, 1614 Medical Arts Bldg., Omaha.
Secretary-Treasurer: Dr. J. H. Murphy, 915 Medical Arts Bldg., Omaha.
Place: As announced by committee. Time: Third Thursday of each month from October to June, inclusive. Dinner at 6 p. m.

North Carolina Pediatric Society

President: Dr. Leroy J. Butler, 405 N. Spring St., Winston-Salem.
Secretary: Dr. C. A. Street, 405 N. Spring St., Winston-Salem.

Oklahoma State Pediatric Society

President: Dr. Julian Feild, 610 S. Monroe St., Enid.
Secretary: Dr. B. H. Nicholson, 301 N. W. Twelfth St., Oklahoma City.

Pennsylvania Medical Society, Pediatric Section

Chairman: Dr. Joseph Stokes, Children's Hospital, Philadelphia.
Secretary: Dr. Theodore O. Elterich, 310 Medical Arts Bldg., Pittsburgh.

South Carolina Pediatric Society

President: Dr. Leland B. Salters, 317 S. Warley St., Florence.
Secretary-Treasurer: Dr. D. Lesesne Smith Jr., 187 Oakland Ave., Spartanburg.

Tennessee State Pediatric Society

President: Dr. Joe T. Smith, 702 Medical Arts Bldg., Knoxville.
Secretary: Dr. Kinsey M. Buck, 1193 Madison Ave., Memphis.

Texas Pediatric Society

President: Dr. George B. Cornick, 507½ E. Houston St., San Antonio.
Secretary-Treasurer: Dr. F. H. Lancaster, 1507 Medical Arts Bldg., Houston.

Virginia Pediatric Society

President: Dr. Basil B. Jones, 1028 W. Franklin St., Richmond.
Secretary: Dr. W. A. McGee, 616 W. Grace St., Richmond.

West Virginia State Medical Society, Section on Pediatrics

President: Dr. John T. Thornton, 58, 16th St., Wheeling.
Secretary: Dr. Claude L. Holland, 400 Locust Ave., Fairmont.

LOCAL

Academy of Medicine of Cleveland, Pediatric Section

Chairman: Dr. J. D. Pilcher, City Hospital, Cleveland.
Secretary: Dr. William M. Champion, 2323 Prospect Ave., Cleveland.
Place: Cleveland Medical Library Bldg. Time: October, December, February and April.

Academy of Medicine, Toronto, Section of Pediatrics

President: Dr. T. B. Verner, 170 St. George St., Toronto.
Secretary: Dr. D. V. Hutton, 170 St. George St., Toronto.

Bronx Pediatric Society

President: Dr. Daniel J. Dolan, 420 E. 159th St., New York.
Secretary: Dr. Samuel T. Levethan, 254 E. 184th St., New York.
Place: Concourse Plaza Hotel, 161st St. and Grand Concourse. Time: Every second Wednesday of each month, except June, July, August and September.

Brooklyn Academy of Pediatrics

President: Dr. Thurman B. Givan, 115 Remsen St., Brooklyn.
Secretary: Dr. John A. Monfort, 861 Carroll St., Brooklyn.
Place: Kings County Medical Society Bldg. Time: Fourth Wednesday of each month, except May, June, July, August and September.

Central New York Pediatric Club

President: Dr. Frank Vasder Bogert, 111 Union St., Schenectady.
Secretary: Dr. Frank J. Williams, 58 S. Swan St., Albany.
Place: Various cities in New York. Time: Third Thursday of April and September.

Chicago Pediatric Society

President: Dr. Robert Black, Del Prado Hotel, Chicago.
Secretary: Dr. James H. Wallace, 715 Lake St., Oak Park, Ill.
Place: Children's Memorial Hospital, 710 Fullerton Ave. Time: Third Tuesday of each month, October to May, inclusive.

Dallas Pediatric Society

President: Dr. John Young, 3930 McKinney Ave., Dallas, Texas.
Secretary-Treasurer: Dr. John E. Ashby, 3622 Fairmount Ave., Dallas, Texas.
Place: Bradford Baby Hospital. Time: 1 p. m., second and fourth Saturdays of each month.

Detroit Pediatric Society

President: Dr. Edward A. Wishropp, 10 Peterboro St., Detroit.
Secretary: Dr. W. J. Scott, 5140 Second Ave., Detroit.
Place: Wayne County Medical Society. Time: 8:30 p. m., first Wednesday of each month from October to June, inclusive.

Fulton County Medical Society, Pediatric Section (Atlanta, Ga.)

Chairman: Dr. Joseph Yampolsky, 478 Peachtree St., Atlanta.
Secretary: Dr. T. I. Willingham, 384 Peachtree St., Atlanta.
Place: Academy of Medicine, 38 Prescott St., N. E. Time: Second Thursday of each month from October to April, 8 p. m.

Hezekiah Beardsley Pediatric Club of Connecticut

President: Dr. H. W. Brayton, 179 Allyn St., Hartford.
Secretary: Dr. Ernest Caulfield, 683 Asylum Ave., Hartford.

Houston Pediatric Society

President: Dr. Walter F. Qualtrough, 920 Westheimer Ave., Houston, Texas.
Secretary-Treasurer: Dr. Allan Bloxsom, 4402 Travis St., Houston, Texas.
Place: Houston Club. Time: Third Monday of each month.

Intermountain Pediatric Society

President: Dr. Eugene Smith, 385 Twenty-Fourth St., Ogden, Utah.
Secretary-Treasurer: Dr. W. C. Cheney, 837 Boston Bldg., Salt Lake City, Utah.
Place: Salt Lake City, General Hospital. Time: First Thursday of each month, 8 p. m.

Kansas City (Missouri) Pediatric Society

President: Dr. W. R. Moore, 620 Francis St., St. Joseph.
Secretary: Dr. F. S. Hogue, 1103 Grand Ave., Kansas City.
Place: Kansas City General Hospital. Time: On call.

Los Angeles County Medical Association, Pediatric Section

President: Dr. George P. Laton, 1136 W. 6th St.
Secretary-Treasurer: Dr. Edwin F. Patton, 3875 Wilshire Blvd., Los Angeles.
Place: Los Angeles County Medical Headquarters, 1925 Wilshire Blvd.
Time: Second Monday of February, April, June, October and December.

Medical Society of the County of Kings and the Academy of Medicine of Brooklyn, Pediatric Section

President: Dr. Harry Apfel, 988 Park Pl., Brooklyn.
Secretary: Dr. Max Palinsky, 1270, 45th St., Brooklyn.
Place: 1313 Bedford Ave., Brooklyn. Time: Third Wednesday of each month, October to May.

Medical Society of the County of Queens, Inc., Section on Pediatrics

Chairman: Dr. W. C. A. Steffen, 42 Union St., Flushing, N. Y.
Secretary-Treasurer: Dr. Edith A. Mittell, 144, 38th Ave., Flushing, N. Y.
Place: Queens County Medical Bldg., Forest Hills, N. Y. Time: Third Monday of October, January, March and May.

Memphis Pediatric Society

President: Dr. W. D. Mims, 1042 Madison Ave., Memphis, Tenn.
Secretary-Treasurer: Dr. W. R. Graves, 1193 Madison Ave., Memphis, Tenn.
Place: Memphis General Hospital. Time: Second Tuesday of each month, except June, July and August, 8 p. m.

Milwaukee Pediatric Society

President: Dr. George F. Kelly, 425 E. Wisconsin St., Milwaukee.
Secretary: Dr. Helen Jane Zillmer, 781 N. Jefferson St., Milwaukee.
Place: Children's Hospital. Time: Second Wednesday of each alternate month, beginning with February.

New England Pediatric Society

President: Dr. Paul Emerson, 319 Longwood Ave., Boston.
Secretary-Treasurer: Dr. Henry E. Gallup, 66 Commonwealth Ave., Boston.
Place: Boston Medical Library. Time: Four meetings a year, occurring from September to May.

New York Academy of Medicine, Section of Pediatrics

Chairman: Dr. Alexander T. Martin, 107 E. 85th St., New York.
Secretary: Dr. Philip M. Stimson, 25 Claremont Ave., New York.
Place: New York Academy of Medicine, 2 E. 103d St. Time: Second Thursday of each month from October to May, inclusive, 8:30 p. m.

Northwestern Pediatric Society

President: Dr. A. V. Stoesser, University Hospital, Minneapolis.
Secretary: Dr. Roger L. J. Kennedy, Mayo Clinic, Rochester, Minn.
Place: Minneapolis, St. Paul, Duluth and Rochester. Time: January, April, July and October.

Philadelphia Pediatric Society

President: Dr. H. H. Perlman, 1904 N. Franklin St., Philadelphia.
Secretary: Dr. James E. Bowman, 4091 Comly St., Philadelphia.
Place: College of Physicians, 19 S. 22d St. Time: Second Tuesday of each month from October to June, inclusive.

Pittsburgh Pediatric Society

President: Dr. James LeRoy Foster, Highland Bldg., Pittsburgh.
Secretary-Treasurer: Dr. E. R. McClusky, 3200 Fifth Ave., Pittsburgh.
Place: Pittsburgh Academy of Medicine. Time: Second Friday, alternate months from October to April, inclusive.

Richmond Pediatric Society

President: Dr. Lee E. Sutton, Jr., 2601 Grove Ave., Richmond, Va.
Secretary-Treasurer: Dr. Louise Fry Galvin, 2416 Stuart Ave., Richmond, Va.
Place: Richmond Academy of Medicine, 1200 E. Clay St. Time: First Thursday of each month (except July, August and September).

Rochester Pediatric Society

President: Dr. F. W. Bush, 29 N. Goodman St., Rochester, N. Y.
Secretary: Dr. David Wolin, 16 N. Goodman St., Rochester, N. Y.
Place: Arranged by program committee. Time: Second Friday of each month.

ROCKY MOUNTAIN PEDIATRIC SOCIETY

President: Dr. Ralph Verploeg, 1850 Gilpin St., Denver.
Secretary: Dr. Max M. Ginsburg, Metropolitan Bldg., Denver.
Place: Children's Hospital, Denver. Time: First Saturday of each month from September to May, inclusive, 2:30 p. m.

ST. LOUIS PEDIATRIC SOCIETY

President: Dr. John Zahorsky, 536 N. Taylor Ave., St. Louis.
Secretary-Treasurer: Dr. Max Deutch, 634 N. Grand Blvd., St. Louis.
Place: St. Louis Medical Society. Time: Third Friday of every month.

SEATTLE PEDIATRIC SOCIETY

President: Dr. Frank H. Douglass, Medical Dental Bldg., Seattle.
Secretary: Dr. C. Lu Verne Smith, Stimson Bldg., Seattle.
Place: College Club. Time: Third Friday of each month, 6:30 p. m.

SOUTHWESTERN PEDIATRIC SOCIETY

President: Dr. Howard R. Cooder, 3875 Wilshire Blvd., Los Angeles.
Secretary: Dr. Philip E. Rothman, 3875 Wilshire Blvd., Los Angeles.
Place: University Club of Los Angeles. Time: First Wednesday in January, March, May September and November.

UNIVERSITY OF MICHIGAN PEDIATRIC AND INFECTIOUS DISEASE SOCIETY

President: Dr. M. Cooperstock, Northern Michigan Children's Clinic, Marquette.
Secretary: Dr. D. Murray Cowie, University of Michigan, Ann Arbor, Mich.

WESTCHESTER COUNTY MEDICAL SOCIETY, PEDIATRIC SECTION (NEW YORK)

President: Dr. Louis V. Waldron, 149 N. Broadway, Yonkers, N. Y.
Secretary-Treasurer: Dr. Fairfax Hall, 421 Huguenot St., New Rochelle, N. Y.
Place: Grasslands Hospital. Time: Third Thursday, October, December, February and April.